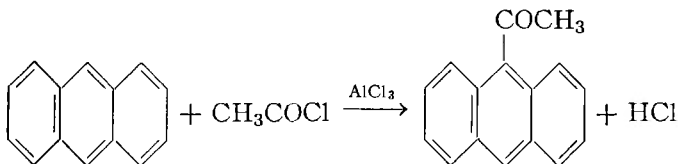


VISIT...

LANZAROTE
Caliente.COM

9-ACETYLANTHRACENE

(Ketone, 9-anthryl methyl)



Submitted by CHARLES MERRITT, JR., and CHARLES E. BRAUN.
Checked by WILLIAM S. JOHNSON and RALPH F. HIRSCHMANN.

1. Procedure

Fifty grams (0.28 mole) of purified anthracene (Note 1) is suspended in 320 ml. of anhydrous benzene and 120 ml. (1.68 moles) of reagent grade acetyl chloride contained in a 1-l. three-necked flask. The flask is fitted with a thermometer which is immersed in the suspension, a calcium chloride drying tube, an efficient motor-driven sealed stirrer, and a rubber addition tube to which a 125 ml. Erlenmeyer flask containing 75 g. (0.56 mole) of anhydrous aluminum chloride is attached.¹

The flask is surrounded by an ice-calcium chloride cooling mixture, and the aluminum chloride is added in small portions from the Erlenmeyer flask at such a rate that the temperature is maintained between -5° and 0° . After the addition is complete, the mixture is stirred for an additional 30 minutes, and the temperature is then allowed to rise slowly to 10° . The red complex which forms is collected with suction on a sintered-glass funnel and washed thoroughly with dry benzene (Note 2). The complex is added in small portions by means of a spatula with stirring to a 600 ml. beaker nearly filled with a mixture of ice and concentrated hydrochloric acid. The mixture is then allowed to come to room temperature, and the crude ketone is collected on a suction filter.

The product is digested under reflux for about 20 minutes with 100–150 ml. of boiling 95% ethanol. The suspension (Note 3) is then cooled quickly almost to room temperature and filtered rapidly with suction to remove any anthracene. The 9-acetyl-anthracene, which separates in the filtrate, is redissolved by heating and allowed to crystallize by slowly cooling the solution (finally to 0–5° in an icebox) (Note 4). A second recrystallization from 95% ethanol yields 35–37 g. (57–60%) of light-tan granules of 9-acetylanthracene melting at 75–76° (Note 5).

2. Notes

1. The Eastman Kodak Company grade melting at 214–215° is satisfactory. Technical anthracene can be purified by codistillation with ethylene glycol (ref. 1, p. 345, footnote 13).

2. A regular Büchner funnel fitted with a mat of glass wool can be employed successfully. The filtration should be carried out as rapidly as possible, and the hydrolysis should be performed immediately thereafter if the humidity is high to minimize reaction on the funnel.

3. Most of the unreacted anthracene remains undissolved as a brown fluffy residue.

4. If the product has a tendency to separate as an oil, the addition of more solvent followed by heating to redissolve the material and subsequent cooling will usually yield a crystalline product.

5. Lüttringhaus and Kacer ² reported the melting point as ca. 80°, but May and Mosettig ³ have found it to be 74–76°.

3. Methods of Preparation

The procedure described is essentially that of Lüttringhaus and Kacer ² except for the method of isolation of the product, which is due to May.⁴

¹ Fieser, *Experiments in Organic Chemistry*, 2nd ed., p. 311, Fig. 39, D. C. Heath and Company, 1941.

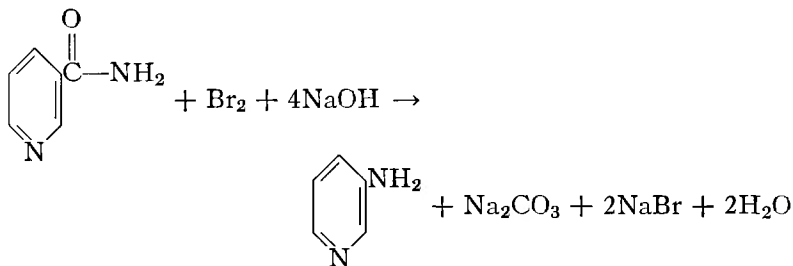
² Lüttringhaus and Kacer, Ger. pat. 493,688 [C. A., **24**, 2757 (1930)].

³ May and Mosettig, *J. Am. Chem. Soc.*, **70**, 686 (1948).

⁴ May, private communication.

3-AMINOPYRIDINE

(Pyridine, 3-amino-)



Submitted by C. F. H. ALLEN and CALVIN N. WOLF.

Checked by CLIFF S. HAMILTON and MARJORIE DEBRUNNER.

1. Procedure

In a 2-l. beaker equipped with a mechanical stirrer and immersed in an ice-salt bath is placed a solution of 75 g. (1.87 moles) of sodium hydroxide in 800 ml. of water. To the solution is added, with stirring, 95.8 g. (30.2 ml., 0.6 mole) of bromine. When the temperature of the solution reaches 0°, 60 g. (0.49 mole) of nicotinamide (Note 1) is added all at once with vigorous stirring. After being stirred for 15 minutes, the solution is clear. The ice-salt bath is replaced by a bath containing water at 75°, and the solution is stirred and heated at 70–75° for 45 minutes.

The solution is cooled to room temperature, saturated with sodium chloride (about 170 g. is required), and extracted with ether in a continuous extractor (Note 2). The extraction time is 15–20 hours. The ether extract is adjusted to a volume of 1 l., dried over 4–5 g. of sodium hydroxide pellets, and filtered, and the ether is removed by distillation from a steam bath. The residue crystallizes on cooling. The yield of dark red crystals melting at 61–63° is 39–41 g. (83–89%).

The crude product is dissolved in a mixture of 320 ml. of benzene and 80 ml. of ligroin (b.p. 60–90°) and heated on a steam bath with 5 g. of Norit and 2 g. of sodium hydrosulfite for 20

minutes. The hot solution is filtered by gravity, allowed to cool slowly to room temperature, and then chilled overnight in a refrigerator. The product is isolated by gravity filtration (Note 3), washed on the filter with 25 ml. of ligroin, and dried in a vacuum desiccator. The yield of white crystals melting at 63–64° amounts to 28–30 g. (61–65%). By concentrating the combined filtrate and washings to a volume of 150 ml., an additional 2–3 g. of pale yellow crystals melting at 62–64° can be obtained. The total yield of 3-aminopyridine is 30–33 g. (65–71%).

2. Notes

1. The nicotinamide should be finely powdered to facilitate rapid solution.

2. The continuous extractor described by Pearl¹ was used. If the material is extracted in a separatory funnel, four 800-ml. portions and ten 500-ml. portions of ether are required to give the above yield.

3. Since 3-aminopyridine is somewhat hygroscopic, it tends to liquefy if collected on a suction filter.

3. Methods of Preparation

3-Aminopyridine has been prepared by heating nicotinamide in an alkaline potassium hypobromite solution at 70°;^{2,3} by hydrolysis of β -pyridylurethan with oleum;⁴ by heating 3-aminopyridine-2-carboxylic acid at 250°;⁵ by reduction of 3-nitropyridine with zinc and hydrochloric acid;⁶ and by heating 3-bromopyridine with ammonia and copper sulfate in a sealed tube.^{7,8}

¹ Pearl, *Ind. Eng. Chem., Anal. Ed.*, **16**, 62 (1944).

² Camps, *Arch. Pharm.*, **240**, 354 (1902).

³ Philips, *Ann.*, **288**, 263 (1895).

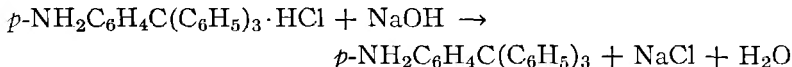
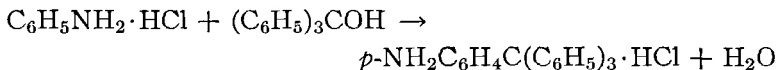
⁴ Curtius and Mohr, *Ber.*, **31**, 2494 (1898).

⁵ Gabriel and Colman, *Ber.*, **35**, 2833 (1902).

⁶ Binz and R  th, *Ann.*, **486**, 95 (1931).

⁷ Maier-Bode, *Ber.*, **69**, 1534 (1936).

⁸ Gitsels and Wibaut, *Rec. trav. chim.*, **60**, 176 (1941).

p*-AMINOTETRAPHENYLMETHANE*(*p*-Toluidine, α,α,α -triphenyl-)**

Submitted by BENJAMIN WITTEN and E. EMMET REID.

Checked by RICHARD T. ARNOLD and JEROME J. ROSENBAUM.

1. Procedure

Into a 1-l. round-bottomed flask equipped with a reflux condenser are introduced 100 g. (0.385 mole) of technical grade triphenylcarbinol (Note 1), 105 g. (0.81 mole) of dry aniline hydrochloride (Note 2), and 250 ml. of glacial acetic acid. The mixture is heated at the reflux temperature for 3 hours. During the period of reflux a clear brown homogeneous solution is formed. The solution while still hot is poured with stirring into a 4-l. beaker containing 2 l. of water. *p*-Aminotetraphenylmethane hydrochloride, which is not very soluble in water, separates as a light-brown solid. It is collected on a Büchner funnel and washed with 1 l. of water. The solid is then put back into the beaker, and a solution of 40 g. of sodium hydroxide in 2 l. of water is added. The mixture is heated to boiling for 1 hour to convert the hydrochloride to the free base (Note 3), which likewise is not very soluble in water. The mixture is allowed to cool to room temperature and is filtered with suction through a Büchner funnel. The solid material is washed with 500 ml. of water and is dried in an oven at 110–120°. The crude substance melts at 243–247°. It is purified by crystallization from 1.7 l. of toluene. The purified product (90–95 g., 70–74%) melts at 249–250° (Note 4).

2. Notes

1. Technical grade triphenylcarbinol is satisfactory, provided it is dry. The checkers obtained a final product having a higher melting point by starting with Eastman Kodak Company purest grade triphenylcarbinol.

2. The aniline hydrochloride must be dry if a good yield of product is to be obtained. Aniline hydrochloride can be prepared conveniently by mixing 75 g. of aniline and 80 ml. of concentrated hydrochloric acid in an evaporating dish and evaporating to dryness. The aniline hydrochloride should be dried in an oven at 110–120° before use. Aniline hydrochloride (Merck) which has been washed with ether and dried at 110–120° can be employed satisfactorily.

3. The mixture tends to bump during the period of heating. This bumping can be overcome by stirring the solution mechanically.

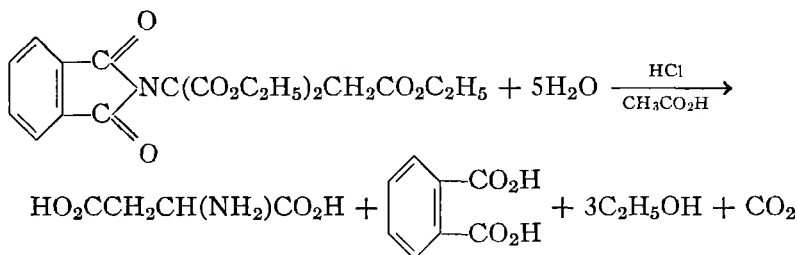
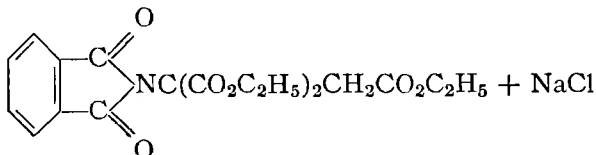
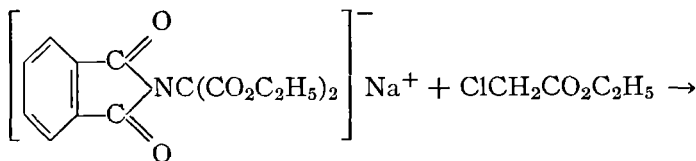
4. A product melting at 256–257° (uncor.)¹ was obtained by the checkers (Note 1).

3. Method of Preparation

The procedure given is similar to one described by Ullmann and Münzhuber,¹ except that one-half as much aniline hydrochloride and two-thirds as much glacial acetic acid are used, and the time of reflux is reduced from 6 to 3 hours. *p*-Aminotetraphenylmethane also can be prepared from triphenylchloromethane and aniline hydrochloride, following the same procedure outlined for triphenylcarbinol and aniline hydrochloride, except that a reaction time of 1 hour is sufficient.;

¹ Ullmann and Münzhuber, *Ber.*, **36**, 407 (1903).

DL-ASPARTIC ACID



Submitted by M. S. DUNN and B. W. SMART.
 Checked by H. T. CLARKE and W. PEARLMAN.

1. Procedure

A. Triethyl α -phthalimidoethane- α,α,β -tricarboxylate. Three hundred and twenty-seven grams (1.0 mole) of diethyl sodium phthalimidomalonate¹ and 735 g. (6.0 moles) of ethyl chloroacetate (b.p. 144–145°) are placed in a 2-l. Claisen flask fitted with a reflux condenser and rubber stoppers. The mixture is heated under reflux in an oil bath at 150–160° for 2.25 hours. The excess ethyl chloroacetate is removed by distillation at 30 mm. until the heating bath temperature reaches 150° and no more distillate is obtained (Note 1). The brown residual mass is

cooled and then extracted with 1250 ml. of ether. The oil dissolves, leaving a solid residue which is separated by filtration and washed with 750 ml. of ether. The combined ether extracts are distilled to remove ether, and the residual oil is heated on a steam bath under reduced pressure (35 mm.) to remove traces of ethyl chloroacetate. The yield of triethyl α -phthalimidoethane- α,α,β -tricarboxylate, dried at 45° for 48 hours, is 373–389 g. (95–99%) (Note 2).

B. DL-Aspartic acid. A mixture of 383 g. of the above crude product, 1 l. of concentrated hydrochloric acid, 1 l. of glacial acetic acid, and 1 l. of water is boiled under reflux in a 5-l. round-bottomed flask for 2–3 hours. The reflux condenser is then replaced by a fractionating column, and the mixture is slowly distilled until the temperature at the head of the column has risen to 108°. This requires about 13 hours. The distillate amounts to 1.5 l. (Note 3).

The residual mixture is allowed to cool, and the phthalic acid which crystallizes is removed by filtration and washed with 350 ml. of 1% hydrochloric acid (Note 4). The combined filtrate and washings are distilled nearly to dryness on a steam bath under reduced pressure; the bulk of the hydrochloric and acetic acids remaining is removed by slowly adding 300 ml. of water through a dropping funnel while the distillation under reduced pressure is continued. The dark brown residue is warmed on a steam bath with 700 ml. of water, is allowed to cool, and is filtered to remove a small amount of black insoluble matter. The filtrate is decolorized with 2 g. of Norit, 200 ml. of hot water being used to wash the Norit. The volume of the combined filtrate and washings, amounting to about 1.2 l., is measured accurately, and a small aliquot portion is analyzed for chloride (Note 5). An amount of pyridine corresponding exactly to the chloride content is added, diluted with 500 ml. of 95% ethanol. The DL-aspartic acid, which crystallizes at once, is separated by filtration after the mixture has stood for 24 hours at room temperature and is washed with 50–100 ml. of cold water (Note 6).

The crude DL-aspartic acid, amounting to 58–60 g., is recrystallized from 600 ml. of hot water and yields 54 g. of pure DL-

aspartic acid. The mother liquors on evaporation to about 90 ml. yield an additional 2–3 g. (Note 7). The total yield of pure colorless DL-aspartic acid is 56–57 g. (42–43%) (Note 8).

2. Notes

1. From 490 to 536 g. of ethyl chloroacetate (b.p. 144–145°) is recovered by the distillation.

2. Although this product cannot be purified by distillation, it contains almost the theoretical amount of nitrogen as shown by Kjeldahl analysis.

3. During the first few hours the distillate contains ethyl acetate; the distillate obtained during the first hour, amounting to 137 ml., distils below 99° and on saturation with sodium chloride yields 115 ml. of crude ethyl acetate.

4. The phthalic acid so obtained is brown and weighs 140–150 g.

5. The total amount of chloride found should be less than 1 mole.

6. The mother liquor contains too little DL-aspartic acid to justify its recovery. When the filtrate and washings are evaporated to a syrup and treated with 500 ml. of 95% ethanol, the pyridine hydrochloride dissolves completely, leaving 8–9 g. of crude glycine which yields little or no sparingly soluble DL-aspartic acid on treatment with a minimum quantity of cold water.

7. The final mother liquor from the recrystallization of DL-aspartic acid yields a small quantity (about 0.5 g.) of glycine.

8. The purity of the recrystallized DL-aspartic acid was established by nitrogen analysis by the Kjeldahl and Van Slyke methods. The decomposition point of this product is 325–348°.

3. Methods of Preparation

The above method for the preparation of DL-aspartic acid is a modification of one described by Dunn and Smart.² Other methods are: the decomposition of acid ammonium malate by

heat,³ the racemization of active aspartic acid⁴ and active asparagine;⁵ the reaction of maleic and fumaric acids with ammonia in a closed tube;⁶ the reduction of oxalacetic ester oxime;⁷ the reduction of silver fumarate by hydroxylamine hydrochloride;⁸ the reduction of nitrosuccinic ester;⁹ the catalytic reduction and amination of oxalacetic acid;¹⁰ and the hydrolysis of triethyl α -aminoethane- α,α,β -tricarboxylate.¹¹

¹ *Org. Syntheses* Coll. Vol. 2, 384 (1943).

² Dunn and Smart, *J. Biol. Chem.*, **89**, 41 (1930).

³ Dessaignes, *Compt. rend.*, **30**, 324 (1850); **31**, 432 (1850); Wolff, *Ann.*, **75**, 293 (1850).

⁴ Michael and Wing, *Ber.*, **17**, 2984 (1884); *Am. Chem. J.*, **7**, 278 (1885).

⁵ Piutti, *Ber.*, **19**, 1691 (1886).

⁶ Engel, *Compt. rend.*, **104**, 1805 (1887); **106**, 1734 (1888); Stadnikoff, *Ber.*, **44**, 14 (1911).

⁷ Piutti, *Gazz. chim. ital.*, **17**, 519 (1887).

⁸ Tanatar, *Ber.*, **29**, 1477 (1896).

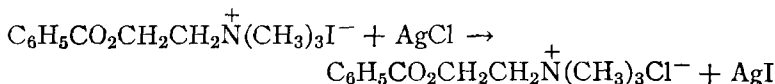
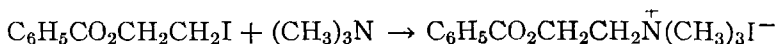
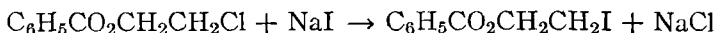
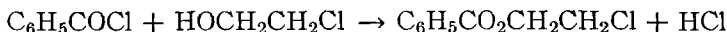
⁹ Schmidt and Widmann, *Ber.*, **42**, 497 (1909).

¹⁰ Knoop and Oesterlin, *Z. physiol. Chem.*, **148**, 294 (1925).

¹¹ Keimatsu and Kato, *J. Pharm. Soc. Japan*, **49**, 111 (1929) [*C. A.*, **24**, 70 (1930)].

BENZOYLCHOLINE IODIDE AND CHLORIDE

(Choline, chloride benzoate, and Choline, iodide benzoate)



Submitted by A. H. FORD-MOORE.

Checked by R. L. SHRINER and CALVIN N. WOLF.

1. Procedure

A. *2-Chloroethyl benzoate*. In a 500-ml. round-bottomed flask attached to a 100-cm. air condenser by a ground-glass joint are placed 80.5 g. (65 ml., 1 mole) of redistilled ethylene chlorohydrin (b.p. 128-129°) and 140.5 g. (115.5 ml., 1 mole) of benzoyl chloride. The apparatus is set up in a good hood, and the mixture is warmed gently with a low flame until the reaction starts (Note 1). The source of heat is withdrawn until the reaction moderates and is then again applied for an additional 30 minutes, during which time the temperature rises to about 200-215°. The flask is fitted with a short column (about 20 cm.) and arranged for distillation. After volatile material has been removed by evacuation with a water pump at a bath temperature of 100-110° the residual liquid is fractionated under reduced pressure. The yield of 2-chloroethyl benzoate boiling at 101-104°/2 mm. is 165-168 g. (89-91%), n_D^{19} 1.5298.

B. *2-Iodoethyl benzoate*. A mixture of 170 g. of anhydrous sodium iodide and 1.2 l. of methyl ethyl ketone (Note 2) is heated on a steam bath for 1 hour with occasional shaking in a 3-l. round-bottomed flask fitted with a water-cooled reflux condenser. 2-Chloroethyl benzoate (162 g., 0.88 mole) is added to the mixture, and heating is maintained for an additional 22-24 hours with occasional shaking. The mixture is cooled to room temperature and filtered through a 15-cm. Büchner funnel with suction. The inorganic salts on the filter are washed with 200 ml. of methyl ethyl ketone, and the filtrate is concentrated by distillation of about 1 l. of the solvent. The residue is poured into 1 l. of water contained in a separatory funnel, which is shaken, and the lower layer is withdrawn. The latter is washed successively with 200 ml. of 10% sodium bisulfite solution, 200 ml. of 5% sodium bicarbonate solution, and 100 ml. of water. It is dried with anhydrous magnesium sulfate (5-7 g.) and fractionated under reduced pressure. The yield of material boiling at 133-136°/2.5 mm., n_D^{15} 1.5820, is 190-196 g. (78-81%).

C. *Benzoylcholine iodide*. A solution of 194 g. (0.70 mole) of 2-iodoethyl benzoate in 200 ml. of dry acetone is treated with

270 ml. of a 19.5% solution of trimethylamine in acetone (Note 3) in a 1-l. Pyrex reagent bottle which is closed with a tightly fitting rubber stopper wired in place. The solution is allowed to stand at room temperature for 24 hours (Note 4), and at the end of this time the quaternary salt is separated by filtration with suction, washed with 200 ml. of dry acetone, and air-dried (Note 5). The weight of the quaternary iodide melting with decomposition at 247° is 200-210 g. (85-90%) (Note 6).

D. *Benzoylcholine chloride*. Silver chloride is prepared by dissolving 160 g. (0.94 mole) of silver nitrate in 500 ml. of boiling distilled water and adding 120 ml. of analytical reagent hydrochloric acid (sp. gr. 1.18) from a dropping funnel in a period of 15 minutes, with continuous stirring. The silver chloride is washed by decantation with three 300-ml. portions of boiling distilled water. The moist silver chloride is suspended in 750 ml. of water warmed to $50-60^{\circ}$ in a 2-l. beaker, and 210 g. (0.63 mole) of benzoylcholine iodide is added in a period of 1 hour, with good mechanical stirring. After the addition is completed, stirring is continued for an additional 30 minutes without the application of heat. The mixture is cooled and filtered with suction. The silver salts on the filter are washed with 200 ml. of hot water (Note 7), and the combined filtrates are evaporated to dryness under reduced pressure (water pump). The residue is dried by twice distilling to dryness with 250 ml. of absolute ethanol and then once with 250 ml. of dry acetone, the last of the acetone being removed under reduced pressure. The product is recrystallized by dissolving it in 240 ml. of isopropyl alcohol (Note 8) and allowing the solution to cool in a refrigerator. It is filtered and dried, first at 100° and then in a vacuum desiccator over silica gel. The yield of pure product, m.p. 207° (dec.), is 125-132 g. (82-87%) (Note 9).

2. Notes

1. Usually the reaction starts at a temperature of 55° to 60° as evidenced by liberation of hydrogen chloride. If the reaction becomes too vigorous it may be moderated by applying a wet towel to the flask.

2. A purified grade of methyl ethyl ketone should be used. The technical material may be purified by allowing it to stand over solid anhydrous calcium chloride for 24 hours, decanting from the syrupy layer and solid through a filter, and then distilling; b.p. 79-80°.

3. The trimethylamine may be generated by the action of alkali on trimethylamine hydrochloride and dissolved in acetone.¹ The submitter prepared trimethylamine by the method of Sommelet and Ferrand² and obtained a 65% yield by the interaction of ammonia, formaldehyde, and formic acid. The checkers found that a commercial 25% solution of trimethylamine in methanol (210 ml.) gave the same yields as the acetone solution.

4. Increasing the reaction period to 48 hours gives an additional 5 to 7 g. of product.

5. If this preparation is carried out during periods of high humidity it is best to place the product in a vacuum desiccator, which is evacuated several times in order to remove the solvent. Anhydrous calcium chloride may be placed in the bottom of the desiccator.

6. This product is quite pure as shown by titration of iodide ion.

7. The silver residues are saved for the recovery of silver³ and iodine.

8. The submitters state that the compound may be recrystallized by boiling with acetone under an upright condenser and adding ethanol cautiously down the condenser until the solid just dissolves. The substance is appreciably soluble in the cold solvent mixture. It is necessary to distil the mother liquor and recrystallize the residue from acetone-ethanol, for otherwise a considerable loss of product will occur. The checkers used isopropyl alcohol for crystallization.

9. Benzoylcholine chloride prepared by this method is pure as shown by titration of ionic chlorine. It is somewhat hygroscopic, though much less so than choline chloride. It is not appreciably hydrolyzed by boiling with water for 1 hour, although more prolonged heating leads to the formation of benzoic acid. Benzoylcholine chloride can be characterized as the picrate, m.p. 177°, formed by treating a strong aqueous solution with an appropriate

amount of 0.5 *N* calcium picrate and crystallizing the product from methyl ethyl ketone.

3. Methods of Preparation

2-Chloroethyl benzoate has been prepared from benzoyl chloride and ethylene chlorohydrin; ^{4,5,6} from benzoic acid, ethylene glycol, and hydrogen chloride ⁷ at 100°; from ethylene oxide and benzoyl chloride; ⁸ from benzoyl chloride and dioxane in the presence of titanium tetrachloride; ⁹ from benzoic acid, ethylene, and chlorine in the presence of various catalysts.¹⁰ It has also been obtained by hydrolysis of 2-chloroethyl benzimidate; ¹¹ by the action of bromomagnesium benzoate on 2-chloroethyl *p*-toluenesulfonate; ¹² and by the action of sodium benzoate on *bis*-(2-chloroethyl) sulfate.¹³

2-Iodoethyl benzoate has been obtained by the action of alcoholic sodium iodide on 2-chloroethyl benzoate.⁴

Benzoylcholine chloride has been prepared by heating choline chloride with benzoyl chloride ¹⁴ and by the action of trimethylamine on 2-chloroethyl benzoate.¹⁵

¹ *Org. Syntheses Coll. Vol. 1*, 528 (1941).

² Sommelet and Ferrand, *Bull. soc. chim. France*, [4] **35**, 446 (1924).

³ *Inorg. Syntheses*, **1**, 2 (1939).

⁴ Zaki, *J. Chem. Soc.*, **1930**, 2271.

⁵ Kirner, *J. Am. Chem. Soc.*, **48**, 2751 (1926).

⁶ Jones and Major, *J. Am. Chem. Soc.*, **49**, 1535 (1927).

⁷ Simpson, *Ann.*, **113**, 120 (1860).

⁸ Altwegg and Landriven, U. S. pat. 1,393,191 [*C. A.*, **16**, 422 (1922)].

⁹ Goldfarb and Smorgonskii, *J. Gen. Chem. U.S.S.R.*, **8**, 1516 (1938) [*C. A.*, **33**, 4593 (1939)].

¹⁰ Brit. pat. 460,720 [*C. A.*, **31**, 4675 (1937)].

¹¹ Gabriel and Neumann, *Ber.*, **25**, 2384 (1892).

¹² Gilman and Beaber, *J. Am. Chem. Soc.*, **45**, 842 (1923).

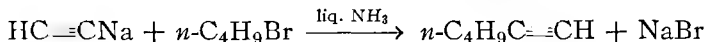
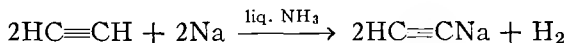
¹³ Suter and Evans, *J. Am. Chem. Soc.*, **60**, 537 (1938).

¹⁴ Nothnagel, *Arch. Pharm.*, **232**, 267 (1894).

¹⁵ Fourneau and Page, *Bull. soc. chim. France*, [4] **15**, 552 (1914).

n-BUTYLACETYLENE

(1-Hexyne)



Submitted by KENNETH N. CAMPBELL and BARBARA K. CAMPBELL.

Checked by R. S. SCHREIBER, M. F. MURRAY, and A. C. OTT.

1. Procedure

Caution! This preparation should be conducted in a hood to avoid exposure to ammonia.

A 5-l. three-necked flask is fitted with an efficient stirrer, mounted through a short glass bushing, and a long gas inlet tube which dips below the surface of the liquid ammonia. The third neck carries a device for holding sodium; this consists of a short piece of 10–12 mm. glass tubing, bent at a 45° angle, through which is passed a 12-in. piece of stout, flexible iron wire (picture wire is satisfactory). The lower end of the wire is attached to a stout iron fish-hook. (Sneck Hook No. 5/0 is satisfactory.)

The flask is charged with about 3 l. of liquid ammonia (Note 1), the stirrer is started, and a rapid stream of acetylene gas (about 5 bubbles per second) is passed in for about 5 minutes to saturate the ammonia. The acetylene from a tank is sufficiently purified by passage through a sulfuric acid wash bottle; a safety trap also should be inserted in the line. Sodium (92 g., 4 gram atoms) is cut in strips (about ½ by ½ by 3 in.) so that they can be inserted through the side neck of the flask. One of these pieces of sodium is attached to the fish-hook and is gradually lowered into the liquid ammonia while a rapid stream of acetylene is passed in. The sodium should be added at such a rate that the entire solution does not turn blue. If it does, the sodium should be raised above the level of the ammonia until the color is discharged (Note 2). The rest of the sodium is added in a similar

manner; the addition requires about 45 minutes, depending on the rate of passage of the acetylene.

The acetylene is shut off, and the gas inlet tube and iron wire are removed, but not the bent glass tubing. A potassium hydroxide tower (Note 3) is attached to the end of this tubing, and a dropping funnel (Note 4) is mounted in the other neck of the flask. *n*-Butyl bromide¹ (548 g., 428 ml., 4.0 moles) is added dropwise with stirring over a period of 45 to 60 minutes (Note 5). The mixture is stirred for an additional 2 hours. Ammonium hydroxide (500 ml.) is then added dropwise, followed by about 1-1.5 l. of distilled water. When the frost on the outside of the flask is loose and can be pulled off easily, the contents of the flask are transferred to a large separatory funnel, and the lower aqueous layer is removed. The organic layer is washed with 100 ml. of distilled water, then with about 100 ml. of 6 *N* hydrochloric acid (the aqueous layer should be tested to make sure that it remains acid; if not, another washing with acid should be carried out), and finally with about 100 ml. of 10% sodium carbonate solution. The material is dried over potassium carbonate, a small amount of solid sodium carbonate is added, and the liquid is fractionated through a helix-packed column of about 10-14 plates. The yield of pure *n*-butylacetylene is 230-252 g. (70-77%); b.p. 71-72°, n_D^{20} 1.3984-1.3990 (Notes 6 and 7).

2. Notes

1. More liquid ammonia should be added from time to time to maintain approximately the same level. Liquid ammonia can be handled in ordinary apparatus, and it is not necessary to use a Dewar flask or to cool the reaction flask in a Dry Ice bath, as a thick frost forms on the outside and partially insulates the contents. In making very volatile alkylacetylenes, such as ethylacetylene and propylacetylene, it is advisable to cool the apparatus in a Dry Ice bath, to minimize loss by entrainment, and to use a Dry Ice condenser. With the higher alkylacetylenes the use of a Dry Ice condenser, as recommended by Henne and

Greenlee,² does not improve the yields enough to justify the extra trouble.

2. In order to see inside the flask a little alcohol may be poured over the outside.

3. This is not absolutely necessary except in damp weather, for the ammonia escaping through the outlet tube prevents the entrance of appreciable amounts of moisture.

4. A calibrated funnel is convenient, as the rate of addition may be judged better.

5. If the addition is carried out more slowly, the yield of product is lowered, unless a Dry Ice condenser is used.

6. The reaction may be carried out on a smaller scale without much loss in yield.

7. Other alkylacetylenes can be made in the same way from primary alkyl bromides. With *n*-propylacetylene the time of addition of *n*-propyl bromide should be about 45 60 minutes, and the yield is lower (40–50%), owing to losses by entrainment unless a Dry Ice condenser is used (b.p. 39 40°; n_D^{20} 1.3850). *n*-Amylacetylene (b.p. 98°; n_D^{20} 1.4088) and isoamylacetylene (b.p. 91–92°; n_D^{20} 1.4060) can be prepared in 70 80% yields by this method; the time of addition of the halide is 1.5 2.0 hours. *n*-Hexylacetylene (b.p. 76–77°/150 mm.; n_D^{20} 1.4157) can be obtained in 65% yields if a 1-mole excess of sodium acetylide is used. The halide is added during the course of 1 hour, and the mixture is stirred for an additional 3 hours before hydrolysis.

The method is not satisfactory for methyl- and ethyl-acetylenes or with secondary and tertiary alkyl halides or with primary alkyl halides above hexyl.

3. Methods of Preparation

n-Butylacetylene is best prepared from *n*-butyl bromide and sodium acetylide in liquid ammonia; ^{2,3} the method described here is a modification of the one published by Vaughn, Vogt, Hennion, and Nieuwland.³ *n*-Butylacetylene also has been prepared from dibromohexanes and alcoholic potassium hydroxide,^{4,5}

from *n*-butyl bromide and ethynylmagnesium bromide at 80–90°,⁶ and from 2-bromo-1-hexene and sodamide in xylene.⁷

¹ *Org. Syntheses* Coll. Vol. 1, 29 (1941).

² Henne and Greenlee, *J. Am. Chem. Soc.*, **67**, 484 (1945).

³ Vaughn, Vogt, Hennion, and Nieuwland, *J. Org. Chem.*, **2**, 1 (1937).

⁴ Welt, *Ber.*, **30**, 1494 (1897).

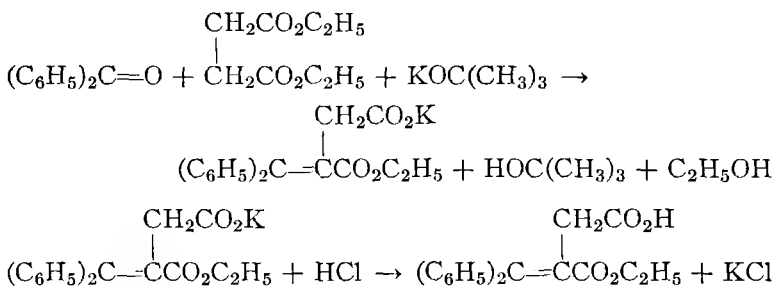
⁵ van Risseghem, *Bull. soc. chim. Belg.*, **35**, 356 (1926).

⁶ Grignard, Lapayre, and Tcheoufaki, *Compt. rend.*, **187**, 519 (1928); **188**, 529 (1929).

⁷ Bourguet, *Ann. chim.*, [10] **3**, 222, 380 (1925).

β-CARBETHOXY-γ,γ-DIPHENYLVINYLAACETIC ACID

(Succinic acid, α-benzhydrylidene-, α-ethyl ester)



Submitted by WILLIAM S. JOHNSON and WILLIAM P. SCHNEIDER.

Checked by ARTHUR C. COPE and MALCOLM CHAMBERLAIN.

1. Procedure

Caution! See Note 3 concerning the safe handling of potassium.

The reaction is conducted in a 500-ml. round-bottomed flask attached (by a ground-glass joint) to a Pyrex reflux condenser, the top of which is connected to a three-way stopcock leading to (a) a source of nitrogen and a mercury trap and (b) a water aspirator (Fig. 1). The flask and condenser are dried by warming with a free flame while the system is under reduced pressure (stopcock turned to (b) to engage aspirator). Dry nitrogen (Note 1) is then admitted to the apparatus by turning the stopcock

slowly to the position indicated in Fig. 1 while nitrogen is bubbling through the mercury trap. The cooled flask is quickly charged with 45 ml. of dry *tert.*-butyl alcohol (Note 2) and 2.15 g. (0.055 gram atom) of potassium (Note 3), and is then reconnected to the apparatus. The flow of nitrogen is stopped, the

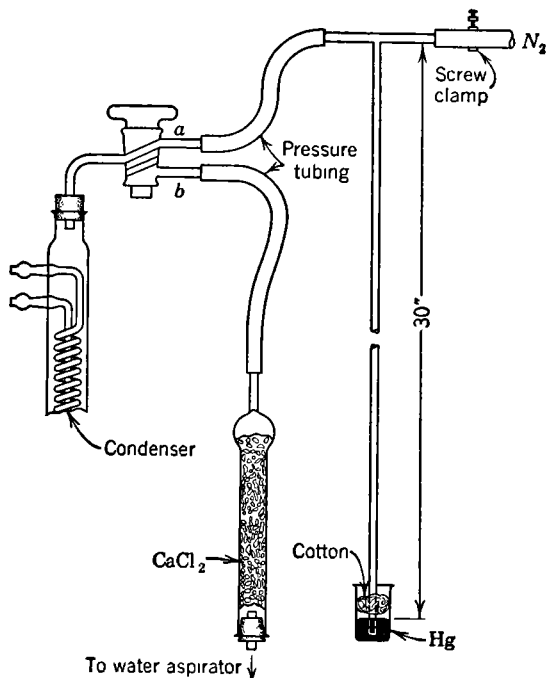


FIG. 1. Apparatus for alternately evacuating and introducing nitrogen into the reaction vessel.

screw clamp is closed, and the mixture is boiled under reflux until the potassium is dissolved (Note 4), hydrogen being liberated through the mercury trap. The solution is then cooled to room temperature while nitrogen is admitted to equalize the pressure. The flask is quickly disconnected just long enough for the addition of 9.11 g. (0.05 mole) of benzophenone (Note 5) and 13.05 g. (0.075 mole) of diethyl succinate (Note 5). The system is then evacuated (until the alcohol begins to boil) and filled with nitrogen. With the stopcock as shown in Fig. 1 and the screw clamp

closed, the mixture is refluxed gently for 30 minutes (Note 6). It is then chilled, acidified with about 10 ml. of cold 1:1 hydrochloric acid, and distilled under reduced pressure (water aspirator) until most of the alcohol is removed. Water is added to the residue, which is extracted thoroughly with ether, and the combined extracts are washed with successive portions of 1 *N* ammonium hydroxide until a test portion gives no precipitate on acidification. The combined alkaline solutions are washed once with a fresh portion of ether and then added slowly with stirring to an excess of cold dilute hydrochloric acid. When the addition is complete the mixture should still be acidic to Congo red. The pale tan crystalline half-ester is separated on a suction funnel, washed well with water, and dried. The yield is 14.0-14.5 g. (90-94%), m.p. 120-124°. If a purer material is desired the product may be recrystallized by dissolving it in about 50 ml. of warm benzene, filtering, and adding an equal volume of petroleum ether (b.p. 40-60°). Upon cooling, 13.0-13.4 g. of almost colorless half-ester crystallizes, m.p. 123-124.5°.

2. Notes

1. Ordinary tank nitrogen is dried satisfactorily by passage through a train consisting of (a) a trap, (b) a wash bottle containing concentrated sulfuric acid, and (c) a drying tube containing fresh soda lime.

2. Commercial *tert*.-butyl alcohol is dried by refluxing with sodium (about 3 g. per 100 ml.) until the metal is about two-thirds dissolved, and then distilling. It may be necessary to add fresh sodium in order to have free metal present throughout the distillation.

3. The following procedure is recommended for the safe handling of potassium. The metal may be cut conveniently under xylene (which has been dried over sodium wire) contained in a mortar. A beaker or crystallizing dish should *not* be used because it is too fragile. Each scrap obtained in cutting off the outer oxide-coated surface of the metal should be immediately transferred with tweezers to a second deep mortar containing dry xy-

lene, where the accumulated residues are decomposed as described below as soon as the cutting operation is completed. In order to weigh the freshly cut metal it may be removed with tweezers, blotted rapidly with a piece of filter paper, and introduced into a tared beaker containing dry xylene. The weighed potassium is then introduced into the reaction mixture, the proper precautions, such as exclusion of air and moisture, rate of addition, etc., being taken, depending on the nature of the reaction involved. *Caution:* It is the small scraps of metal that adhere to the knife or float on top of the xylene that are most likely to start a fire.

Danger! Potassium residues have been known to explode even under a protective liquid. It is therefore important that all such residues be decomposed *immediately*; under no circumstances should they be stored. The mortar containing the scraps is moved to the rear of the hood and *tert.*-butyl (not methyl or ethyl) alcohol is added in small portions from a medicine dropper or beaker at such a rate that the reaction does not become too vigorous. A square sheet of asbestos large enough to cover the mortar should be at hand. If the liquid should catch fire it may be extinguished easily by covering the mortar with the asbestos sheet. There should be no other inflammable material or flames in the hood during this treatment. Sufficient *tert.*-butyl alcohol must be employed to ensure *complete* decomposition of all the potassium. Small specks of potassium usually remain in the first mortar used for the cutting operation; they should be decomposed in the hood by cautious addition of small amounts of *tert.*-butyl alcohol as described above.

4. If the alcohol and apparatus have been properly dried, the dissolution of the potassium will be slow, requiring more than 4 hours of refluxing.

5. Eastman Kodak Company grade material is satisfactory if dried by redistillation.

6. The potassium salt of the half-ester may precipitate during the period of heating.

3. Methods of Preparation

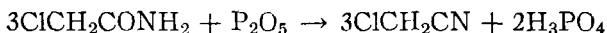
β -Carbethoxy- γ,γ -diphenylvinylacetic acid has been prepared in 58–62% yield by the condensation of benzophenone with diethyl succinate in the presence of sodium ethoxide.¹ The procedure described here is a modification involving the use of potassium *tert.*-butoxide as the condensing agent.²

¹ Stobbe, *Ann.*, **308**, 89 (1899).

² Johnson, Petersen, and Schneider, *J. Am. Chem. Soc.*, **69**, 74 (1947).

CHLOROACETONITRILE

(Acetonitrile, chloro-)



Submitted by D. B. REISNER and E. C. HORNING.

Checked by R. L. SHRINER and CALVIN N. WOLF.

1. Procedure

In a 3-l. round-bottomed three-necked flask fitted with an efficient mechanical stirrer, a reflux condenser, and a thermometer are placed 170 g. (1.2 moles) of phosphorus pentoxide, 187 g. (2 moles) of chloroacetamide¹ (Note 1), and 800 ml. of dry technical trimethylbenzene (Note 2). The mixture is refluxed gently with vigorous stirring for 1 hour. The reaction mixture is then allowed to cool to about 100° with continuous stirring, and the reflux condenser is replaced with a distilling adapter fitted with a thermometer and a water-cooled condenser.

The crude product and part of the solvent are distilled at atmospheric pressure (Note 3). The yield of crude product boiling at 124–128° is 121–131 g. (80–87 %) (n_D^{25} 1.441–1.444). In order to obtain a pure product, the crude chloroacetonitrile is mixed with 10 g. of phosphorus pentoxide and redistilled through an efficient packed fractionating column (Note 4). The yield of

pure chloroacetonitrile distilling at 123–124° is 93–106 g. (61–70%) (Note 5).

2. Notes

1. The practical grade of chloroacetamide obtainable from the Eastman Kodak Company can be used.

2. Technical trimethylbenzene with a boiling range of 166–174° is satisfactory.

3. About 200 ml. of solvent can be recovered. The remainder is left in the flask to facilitate removal of the residue.

4. A Fenske column packed with glass helices previously described in *Organic Syntheses*² is satisfactory. The product has n_D^{20} 1.426, d_4^{20} 1.1896, in good agreement with reported values.³ When a Vigreux column was used the distillate had d_4^{20} 1.072 and n_D^{25} 1.430–1.436, indicating incomplete separation from the trimethylbenzenes (1,3,5-trimethylbenzene has d_4^{20} 0.86; n_D^{25} 1.494).

5. The product can also be distilled under reduced pressure; b.p. 60–61°/100 mm.; 30–32°/15 mm.

3. Methods of Preparation

Practical syntheses of chloroacetonitrile depend upon dehydration of chloroacetamide with phosphorus pentoxide. The present method uses a liquid reaction medium; in previous procedures the dry reagents were heated in the absence of solvent or liquid medium.^{4,5}

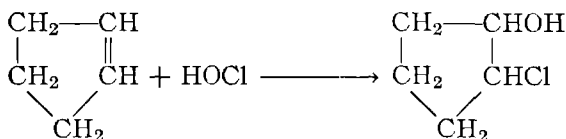
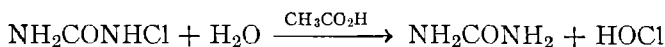
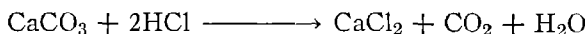
¹ *Org. Syntheses* Coll. Vol. 1, 153 (1941).

² *Org. Syntheses*, 25, 2 (1945).

³ Rogers, *J. Am. Chem. Soc.*, 69, 457 (1947).

⁴ Scholl, *Ber.*, 29, 2417 (1896).

⁵ Steinkopf, *Ber.*, 41, 2540 (1908).

trans*-2-CHLOROCYCLOPENTANOL*(Cyclopentanol, 2-chloro-, *trans*-)**

Submitted by HUGH B. DONAHOE and CALVIN A. VANDERWERF.
 Checked by ARTHUR C. COPE and ELBERT C. HERRICK.

1. Procedure

A mixture of 150 g. (2.5 moles) of urea, 125 g. (1.25 moles) of precipitated calcium carbonate, and 150 ml. of water in a 2-l. three-necked flask is tared and cooled in an ice-salt bath. The flask is equipped with a thermometer which extends into the reaction mixture, a gas inlet tube, an outlet tube leading to a gas-absorption trap,¹ and a slip- or mercury-sealed mechanical stirrer which will disperse chlorine gas below the surface of the liquid (Note 1).

A rapid stream of chlorine gas is bubbled into the mixture at 0–15° with vigorous stirring until an increase in weight of about 95 g. has occurred (30–40 minutes) (Note 2). A 250-ml. portion of water at room temperature is added to the suspension, which is then filtered by suction through rather porous filter paper on a 16-cm. Büchner funnel. The filtrate is removed and cooled in an ice bath, and the filter cake is washed on the funnel with a 250-ml. portion of water at room temperature. The filtrate is poured back in the funnel and sucked through the filter cake repeatedly until no more solid appears to dissolve, and then is combined with the original filtrate (Note 3).

The cold filtrates (solutions of monochlorourea) are transferred to a 3-l. two-necked flask immersed in an ice-salt bath. The flask is equipped with a slip- or mercury-sealed mechanical stirrer and an efficient reflux condenser. To the flask are added 500 g. of ice, 100 ml. of glacial acetic acid, and 136 g. (2.0 moles) of cyclopentene (or 1.43 times the weight increase in grams during introduction of the chlorine) (Note 4). Mechanical stirring is begun, and is continued while the flask is kept packed in ice until the cyclopentene (the top layer) disappears and a heavy oil settles to the bottom (Note 5).

The solution is saturated with sodium chloride and distilled with steam until all the 2-chlorocyclopentanol is collected, which requires distillation of a volume of about 2 l. The distillate is saturated with sodium chloride, the oily layer separated, and the aqueous layer extracted four times with 300-ml. portions of ether. The ether extracts are added to the oil, and the solution is washed with a saturated sodium chloride solution and dried over anhydrous sodium sulfate. The ether is removed by distillation, and the product is distilled under reduced pressure through a total condensation, variable take-off, 15 by 1.5 cm. column packed with glass helices. A trap cooled with Dry Ice is placed in the vacuum line between the column and the pump. Low-boiling fractions, b.p. 43–81°/15 mm., amount to 19–40 g. (Note 6). The *trans*-2-chlorocyclopentanol is collected at 81–82°/15 mm. in a yield of 126–135 g. (52–56%); n_D^{25} 1.4770 (Note 7).

2. Notes

1. Rapid absorption of chlorine depends on efficient stirring and dispersal of the gas through the liquid phase. A stirrer which disperses the gas through the solution by vigorous agitation may be used,² or the gas may be introduced through the stirrer.³

2. The actual weight of chlorine absorbed is equal to the sum of the weight increase noted plus the weight of carbon dioxide formed minus the relatively small weight of carbon dioxide that remains dissolved in the reaction mixture.

3. The combined filtrates may be titrated with 1 *N* sodium thiosulfate solution to determine the yield of monochlorourea.⁴ This preparation of monochlorourea is a modification of procedures previously described.^{4,5}

4. Best yields result when an excess of cyclopentene is used, as specified. The weight increase should be roughly 95 g., and the amount of cyclopentene should be varied proportionately by using 1.43 times the weight increase in grams.

5. The stirring time is about 12-15 hours. It is advantageous to allow the ice to melt and the reaction mixture to come to room temperature during the last 2-3 hours.

6. The fractions boiling at 43-48°/15 mm. and 48-81°/15 mm. contain a mixture of 1,2-dichlorocyclopentane and *cis*- and *trans*-2-chlorocyclopentanol.^{6,7}

7. The yield is based on the weight of cyclopentene, although this reagent is used in slight excess.

3. Methods of Preparation

2-Chlorocyclopentanol has been prepared by the reaction of dry hydrogen chloride with 1,2-cyclopentanediol⁸ and by the addition of hypochlorous acid to cyclopentene.^{6,7,8,9}

¹ *Org. Syntheses* Coll. Vol. **2**, 4 (1943).

² *Org. Syntheses*, **30**, 94 (1950).

³ Russell and Vanderwerf, *Ind. Eng. Chem., Anal. Ed.*, **17**, 269 (1945).

⁴ McRae, Charlesworth, and Alexander, *Can. J. Research*, **21B**, 1 (1943).

⁵ Detoef, *Bull. soc. chim. France*, [4] **31**, 102 (1922).

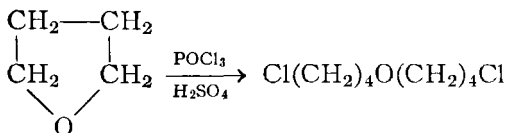
⁶ Rothstein and Rothstein, *Compt. rend.*, **209**, 761 (1939).

⁷ Godchot, Mousseron, and Granger, *Compt. rend.*, **200**, 748 (1935).

⁸ Meiser, *Ber.*, **32**, 2052 (1899).

⁹ Mousseron, Granger, Winternitz, and Combes, *Bull. soc. chim. France*, **1946**, 610.

4,4'-DICHLORODIBUTYL ETHER

[Ether, *bis*(4-chlorobutyl)]

Submitted by KLIEM ALEXANDER and H. V. TOWLES.

Checked by ARTHUR C. COPE, MALCOLM CHAMBERLAIN, and MARK R. KINTER.

1. Procedure

Caution! This preparation should be conducted in a good hood because some hydrogen chloride is evolved.

In a 2-l. three-necked flask fitted with a mercury-sealed stirrer (Note 1), a reflux condenser connected to a calcium chloride tube, and a thermometer is placed 360 g. (406 ml., 5 moles) of dry tetrahydrofuran (Note 2). The flask is surrounded by an ice bath, stirring is started, and 256 g. (153 ml., 1.67 moles) of phosphorus oxychloride is added rapidly. The mixture is cooled to 10–15°, and 50 ml. of concentrated sulfuric acid (sp. gr. 1.84) is added during the course of 3–10 minutes at a rate that does not cause the temperature to rise above 40°. The ice bath is then removed and the mixture is heated cautiously over a low luminous flame until an exothermic reaction becomes evident at about 88–90° (Note 3). By moderate cooling or warming as may be required the temperature is maintained at 90–100° until the exothermic reaction ceases, as indicated by the increased rate of heating required to maintain the reaction temperature, and thereafter for an additional 10 minutes (Note 4). Six hundred milliliters of water is added, the mixture is heated under reflux for 30 minutes and then distilled through a downward condenser until the vapor temperature reaches 99–100° (Note 5).

The dark reaction mixture is cooled to room temperature, transferred to a separatory funnel, and extracted with 225 ml. of ether.

The ether extract is washed with four 100-ml. portions of water and dried over anhydrous sodium sulfate or magnesium sulfate. The mixture is filtered, the ether is removed by distillation, and the residual liquid is fractionated under reduced pressure from a modified Claisen flask. The yield of colorless 4,4'-dichlorodibutyl ether, b.p. 84–86°/0.5 mm. (116–118°/10 mm.), n_D^{25} 1.4562, d_4^{25} 1.0690, is 257–268 g. (52–54% based on tetrahydrofuran) (Note 6).

2. Notes

1. Efficient stirring is necessary to permit good control of the reaction temperature.

2. The same yield of 4,4'-dichlorodibutyl ether was obtained from redistilled tetrahydrofuran dried over sodium or a good-quality commercial grade obtained from the Electrochemicals Department of the E. I. du Pont de Nemours and Company and dried over Drierite.

3. About 30 minutes is required for the temperature to reach 88–90°. The temperature rises rapidly to 76°, at which point refluxing of tetrahydrofuran accompanied by evolution of some hydrogen chloride occurs. Thereafter refluxing gradually diminishes and the temperature increases approximately as follows: 0 minutes, 76°; 5 minutes, 77°; 10 minutes, 78°; 15 minutes, 80°; 20 minutes, 85°; 25 minutes, 94°; 27 minutes, 100°.

4. The temperature is easily kept within the range of 90–100° by occasional cooling with an ice-water bath. Above 100° the reaction tends to become violent, resulting in excessive evolution of hydrogen chloride and a lower yield of the product. The exothermic phase of the reaction is usually complete in 15–20 minutes.

5. Refluxing with water serves to decompose phosphorus-containing complexes and facilitates isolation of the product. The aqueous distillate contains small amounts of 1,4-dichlorobutane and unchanged tetrahydrofuran.

6. The product as obtained with these physical constants is analytically pure.

3. Methods of Preparation

The procedure described is based on one reported by Alexander and Schniepp.¹ 4,4'-Dichlorodibutyl ether has also been prepared by the action of thionyl chloride on tetrahydrofuran² and by heating 4-chlorobutanol and hydrogen chloride under pressure.³

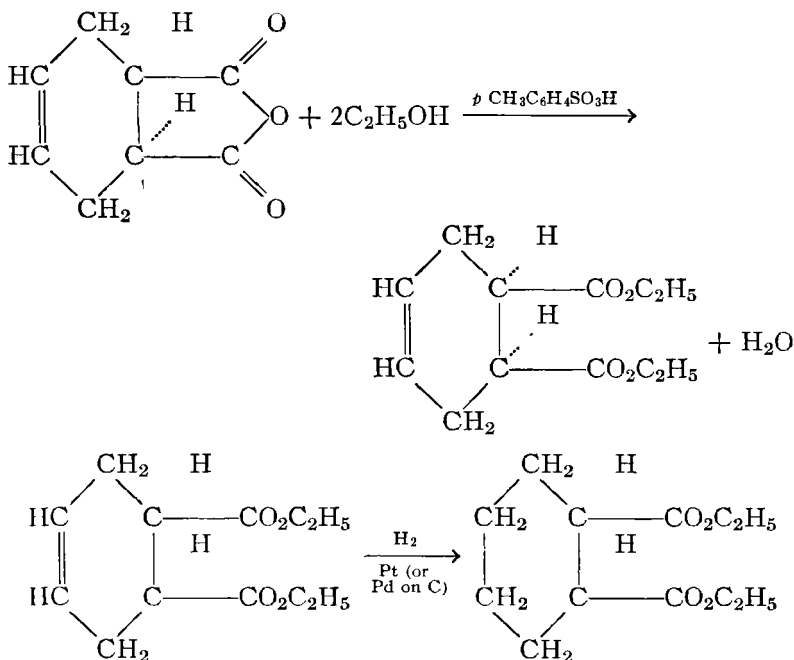
¹ Alexander and Schniepp, *J. Am. Chem. Soc.*, **70**, 1839 (1948).

² Krzikalla and Maier, PB 631, Office of Technical Services, U. S. Department of Commerce

³ Trieschmann, U. S. pat. 2,245,509 [*C. A.*, **35**, 5914 (1941)].

DIETHYL *cis*- Δ^4 -TETRAHYDROPHTHALATE AND DIETHYL *cis*-HEXAHYDROPHTHALATE

(4-Cyclohexene-1,2-dicarboxylic acid, diethyl ester, *cis*-, and
1,2-Cyclohexanedicarboxylic acid, diethyl ester, *cis*-)



Submitted by ARTHUR C. COPE and FLEET C. HERRICK
Checked by CHARLES C. PRICE and GEORGE A. CYPIER

1. Procedure

A. *Diethyl cis- Δ^4 -tetrahydrophthalate*. In a 2-l. round-bottomed flask are placed 228 g. (1.5 moles) of *cis- Δ^4 -tetrahydrophthalic anhydride*,¹ 525 ml. (9 moles) of commercial absolute ethanol, and 2.5 g. of *p*-toluenesulfonic acid monohydrate. The flask is connected to a reflux condenser and heated in an oil bath maintained at 95–105° for 12–16 hours.

At this time 270 ml. of toluene is added to the mixture and the condenser is changed for distillation. An azeotropic mixture of ethanol, toluene, and water is distilled at 75–78° with the bath at 105–110°. When the temperature begins to drop (Note 1), 525 ml. of commercial absolute ethanol is added and the mixture is again heated under reflux for 12–16 hours (Note 2). Again 270 ml. of toluene is added, and the azeotropic mixture is distilled until the vapor temperature falls to 68°. After the residue is cooled, the system is evacuated to 25–35 mm. and the remaining ethanol and toluene are distilled.

The residual liquid is diluted with 200 ml. of ether. The ether solution is washed twice with 100-ml. portions of 3% sodium carbonate solution (Note 3). The combined carbonate solutions are extracted three times with 100-ml. portions of ether, and the ether solutions are combined and washed with 100 ml. of distilled water. The ether solution is dried over magnesium sulfate, filtered, and concentrated, and the residue is distilled under reduced pressure. The yield of product boiling at 129–131°/5 mm., n_D^{25} 1.4605–1.4610, is 280–292 g. (83–86%) (Note 4).

B. *Diethyl cis-hexahydrophthalate*. The reaction is carried out in a low-pressure catalytic hydrogenation apparatus.² In a 500-ml. Pyrex centrifuge bottle are placed 0.5 g. of Adams platinum oxide catalyst (Note 5) and 20 ml. of commercial absolute ethanol (Note 6). The bottle is connected to a calibrated low-pressure hydrogen tank and alternately evacuated and filled with hydrogen twice. Hydrogen is then admitted to the system until the pressure is 1–2 atmospheres (15–30 lb.), and the bottle is shaken for 20–30 minutes to reduce the platinum oxide. The shaker is stopped, the bottle is evacuated, and air is admitted. Two hun-

dred and twenty-six grams (1 mole) of diethyl *cis*- Δ^4 -tetrahydrophthalate is placed in the bottle. The container in which the ester was weighed is rinsed with 10 ml. of absolute ethanol, which is added to the ester. The bottle is alternately evacuated and filled with hydrogen twice. Hydrogen is admitted to the system until the pressure is 25–30 lb. (approximately 2 atmospheres), and the bottle is shaken until the pressure drop indicates that the theoretical amount (1 mole) of hydrogen has been taken up and the absorption ceases (3–5 hours). The bottle is evacuated and then air is admitted. The catalyst is removed by filtration through a small Hirsch funnel. The bottle is washed with 15 ml. of alcohol, which is poured through the funnel. Most of the solvent is distilled at 25–35 mm. Distillation of the residue under reduced pressure yields 215–219 g. (94–96%) of diethyl *cis*-hexahydrophthalate, b.p. 130–132°/9 mm., n_D^{25} 1.4508–1.4510 (Note 7).

2. Notes

1. A period of 5–8 hours is required for this distillation and for the similar subsequent distillation.
2. If the second period of reflux and azeotropic distillation is omitted the yield is decreased to 66%.
3. The product should be washed with sodium carbonate solution until the aqueous solution remains basic.
4. Dimethyl *cis*- Δ^4 -tetrahydrophthalate can be prepared by a similar procedure. *cis*- Δ^4 -Tetrahydrophthalic anhydride (228 g., 1.5 moles) is heated under reflux with 364 ml. (9 moles) of commercial anhydrous methanol and 2.5 g. of *p*-toluenesulfonic acid monohydrate for 12–16 hours. At this time 270 ml. of toluene is added and the mixture is distilled. When the distillation temperature drops from 68–70° to 45°, after about 4–6 hours, 364 ml. of absolute methanol is added and the mixture again is heated under reflux for 12–16 hours. An additional 270 ml. of toluene is added, and distillation is continued for 4–6 hours. The residual liquid is purified by a procedure similar to the one described for the ethyl ester. The yield of dimethyl *cis*- Δ^4 -tetrahydrophthalate, boiling at 120–122°/5 mm., n_D^{25} 1.4700, is 239 g. (80%).

5. The platinum oxide catalyst was obtained from Baker and Company, Newark, New Jersey. Platinum oxide may also be obtained from the American Platinum Works, Newark, New Jersey.

6. The reduction also may be carried out using 1 g. of palladium on carbon,³ in which case no solvent is required and prereduction of the catalyst is unnecessary.

7. Dimethyl *cis*-hexahydrophthalate also may be prepared by a similar reduction of dimethyl *cis*- Δ^4 -tetrahydrophthalate. With 0.5 g. of prereduced Adams platinum oxide catalyst, 198 g. (1 mole) of dimethyl *cis*- Δ^4 -tetrahydrophthalate was reduced to give 196 g. (98%) of dimethyl *cis*-hexahydrophthalate, b.p. 110–112°/5 mm., n_D^{25} 1.4570.

3. Methods of Preparation

Diethyl *cis*-hexahydrophthalate has been prepared from *cis*-hexahydrophthalic acid, absolute ethanol, and sulfuric acid,^{4,5} and from *cis*-hexahydrophthalic anhydride, absolute ethanol, and sulfuric acid.⁶ Diethyl *cis*- Δ^4 -tetrahydrophthalate has been prepared from *cis*- Δ^4 -tetrahydrophthalic acid or its anhydride, ethanol, and sulfuric acid.⁷ Dimethyl *cis*- Δ^4 -tetrahydrophthalate and dimethyl *cis*-hexahydrophthalate have been synthesized by the procedures of this preparation.⁸

¹ *Org. Syntheses*, **30**, 93 (1950).

² Suitable apparatus is described in *Org. Syntheses Coll. Vol. 1*, 61 (1941).

³ *Org. Syntheses*, **26**, 32 (1946).

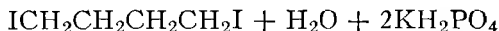
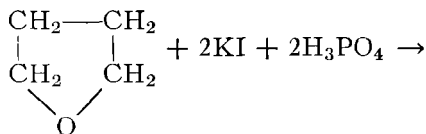
⁴ von Auwers and Ottens, *Ber.*, **57**, 437 (1924).

⁵ Hückel and Goth, *Ber.*, **58**, 447 (1925).

⁶ Price and Schwarcz, *J. Am. Chem. Soc.*, **62**, 2891 (1940).

⁷ Brooks and Cardarelli, U. S. pat. 1,824,069 [*C. A.*, **26**, 152 (1932)].

⁸ Cope and Herrick, *J. Am. Chem. Soc.*, **72**, 983 (1950).

1,4-DIIODOBUTANE**(Butane, 1,4-diiodo-)**

Submitted by HERMAN STONE and HAROLD SCHECHTER.

Checked by CLIFF S. HAMILTON and R. C. RUPERT.

1. Procedure

Tetrahydrofuran (36 g., 0.5 mole) (Note 1) is added to a mixture of potassium iodide (332 g., 2 moles), 85% orthophosphoric acid (231 g., 135 ml., 2 moles), and phosphoric anhydride (65 g.) (Notes 2, 3, and 4) in a 1-l. three-necked flask equipped with a sealed mechanical stirrer, a reflux condenser, and a thermometer. The mixture is stirred and heated at its reflux temperature for 3 hours, during which time a dense oil separates from the acid layer. The stirred mixture is cooled to room temperature, and 150 ml. of water and 250 ml. of diethyl ether are added (Note 5). The ether layer is separated, decolorized with dilute aqueous sodium thiosulfate solution, washed with cold saturated sodium chloride solution, and dried over anhydrous sodium sulfate. The ether is removed by distillation on a steam bath, and the residue is distilled under reduced pressure from a modified Claisen flask. The portion boiling at 108–110°/10 mm. is collected. The yield of colorless 1,4-diiodobutane (n_D^{20} 1.615; d_4^{20} 2.300) (Note 6) is 143–149 g. (92–96%).

2. Notes

1. Tetrahydrofuran was obtained by the submitters from E. I. du Pont de Nemours and Company.

2. The specified mixture of commercial 85% orthophosphoric acid and phosphoric anhydride corresponds to a 95% orthophos-

phoric acid solution. The phosphoric anhydride is placed in the dry flask, and the 85% orthophosphoric acid is added with stirring. After the mixture has cooled to room temperature, solid potassium iodide is added. The solution should be cooled, before addition of the potassium iodide, to prevent evolution of hydrogen iodide and formation of iodine. After the tetrahydrofuran is added, the mixture can be heated as desired since the hydrogen iodide reacts as rapidly as it is formed.

3. Orthophosphoric acid of 95% concentration is most efficient for effecting cleavage of tetrahydrofuran. Commercial orthophosphoric acid (85%) may be used; however, the yield drops to 82% and approximately 10% of the tetrahydrofuran is recovered. Anhydrous orthophosphoric acid and tetraphosphoric acid cannot be employed conveniently because of the limited solubility of hydrogen iodide in these reagents.

4. This procedure has been used successfully to convert simple aliphatic ethers into their corresponding iodides. Yields of iodides obtained in the reaction of di-*n*-butyl ether and diisopropyl ether with potassium iodide and 95% orthophosphoric acid were 81 and 90% respectively. Small quantities of the corresponding alcohols were also isolated as products from these reactions.

5. Usually one extraction with ether is sufficient to decolorize the acid layer; if this fails, an additional extraction with 100 ml. of ether is recommended.

6. The checkers obtained values of: n_D^{25} 1.619; d_4^{26} 2.349. The product darkens slowly on standing.

3. Methods of Preparation

1,4-Diiodobutane has been prepared in 51% yield by the reaction of phosphorus, iodine, and tetrahydrofuran.¹ It has also been prepared by the reaction of hydriodic acid with phenoxybutyl iodide^{2,3} and with the diisoamyl ether of 1,4-butanediol.⁴

¹ Heisig, *J. Am. Chem. Soc.*, **61**, 525 (1939).

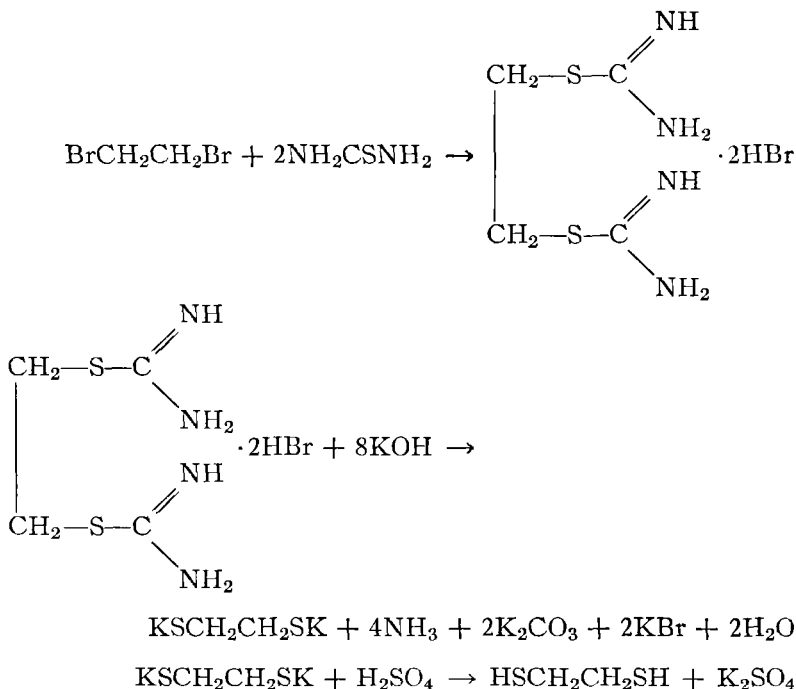
² von Braun and Beschke, *Ber.*, **39**, 4357 (1906).

³ Marvel and Tannenbaum, *J. Am. Chem. Soc.*, **44**, 2650 (1922).

⁴ Hamonet, *Compt. rend.*, **132**, 345 (1901).

ETHANEDITHIOL

(1,2-Ethanedithiol)



Submitted by A. JOHN SPEZIALE.

Checked by R. S. SCHREIBER and R. W. KRATZ.

1. Procedure

Caution! This preparation requires the use of a good hood.

In a 5-l. round-bottomed flask fitted with an efficient reflux condenser are placed 2750 ml. of 95% ethanol and 609 g. (8.0 moles) of thiourea. The mixture is brought to the reflux temperature on a steam bath, and the refluxing solution is almost clear. The steam is turned off, and 751.5 g. (4.0 moles) of ethylene dibromide is added in one portion. Within 5 minutes a vigorous

reaction (Note 1) ensues and ethylene diisothiuronium bromide separates from solution. The exothermic reaction is allowed to continue to completion without further application of heat. The isothiuronium salt is collected by filtration and dried. The salt melts with decomposition at 225–227° (Note 2) and weighs 1104 g. (81%).

Concentration of the filtrate to a volume of about 250 ml. and recrystallization from 95% ethanol of the crude isothiuronium salt which separates gives an additional 130 g. of material. The total yield of the salt is 1234 g. (90%).

A mixture of 255 g. (0.75 mole) of ethylene diisothiuronium bromide and 640 g. (11.4 moles) of potassium hydroxide in 1360 ml. of water is placed in a 5-l. round-bottomed three-necked flask and boiled under reflux for 5 hours. Ammonia is evolved during the reflux period. The flask is then equipped with a separatory funnel, a gas-inlet tube, and a condenser set for steam distillation (Note 3). Nitrogen is admitted through the inlet tube, and a cooled solution of 415 ml. of sulfuric acid in 760 ml. of water is added dropwise (Note 4). The addition is continued until the reaction mixture becomes acid to Congo red paper, and then a 20% excess of acid is added. Approximately 725–850 ml. of the acid solution is required. The heat of neutralization is sufficient to distil part of the dithiol. At the end of the addition of the acid, the passage of nitrogen is discontinued and steam is admitted through the inlet tube. The steam distillation is continued until about 3 l. of distillate is collected. The oil is separated from the water in the distillate, which is then extracted with two 500-ml. portions of ether. The ether solution and the oil are dried separately over calcium chloride. After evaporation of the solvent, the residue is added to the oil and the crude product is fractionated through a 10-in. Vigreux column under reduced pressure in an atmosphere of nitrogen. The ethanedithiol boils at 63°/46 mm. (Note 5) and weighs 39–44 g. (55–62%); n_D^{20} 1.5589.

2. Notes

1. The reaction may be so vigorous that external cooling is required. A cloth wet with ice water and applied to the flask is sufficient to control the reaction.

2. The melting point seems to depend upon the rate of heating. Use of a Fisher-Johns melting-point apparatus gives a value of 240–242°.

3. At this point the reaction *must* be carried out in a good hood. The vapors of ethanedithiol may cause severe headache and nausea.

4. The alkaline solution should be at room temperature before the acidification is begun.

5. In one run the checkers observed a boiling point of 69°/46 mm.

3. Methods of Preparation

Ethanedithiol has been prepared from ethylene dichloride ¹ or ethylene dibromide ² and alcoholic potassium hydrosulfide; from ethylene dibromide and alcoholic sodium hydrosulfide; ³ from ethylene dichloride ⁴ or ethylene dibromide ⁵ and alcoholic sodium hydrosulfide under pressure; from ethylene dibromide and thio-urea; ⁶ and by the catalytic hydrogenation with cobalt trisulfide ⁷ or nickel-on-kieselguhr ⁸ of the mixture resulting from the reaction of ethylene and sulfur. The present method is a modification of one described by Mathias.⁶

¹ Löwig and Weidmann, *Ann.*, **36**, 321 (1840).

² Fasbender, *Ber.*, **20**, 460 (1887).

³ Meyer, *Ber.*, **19**, 3259 (1886).

⁴ Tucker and Reid, *J. Am. Chem. Soc.*, **55**, 775 (1933).

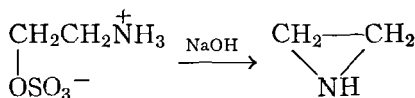
⁵ Simpson, *Can. J. Research*, **25B**, 20 (1947).

⁶ Mathias, *Bol. faculdade filosof., ciênc. e letras, Univ. São Paulo*, **14**, Quim. No. 1, 75 (1942) [*C. A.*, **40**, 2792 (1946)].

⁷ Signaigo, U. S. pat. 2,402,456 [*C. A.*, **40**, 5767 (1946)].

⁸ Lazier, Signaigo, and Wernitz, U. S. pat. 2,402,643 [*C. A.*, **40**, 5764 (1946)].

ETHYLENIMINE



Submitted by C. F. H. ALLEN, F. W. SPANGLER, and E. R. WEBSTER.

Checked by R. S. SCHREIBER, A. C. OTT, and M. F. MURRAY.

1. Procedure

Caution! This preparation should be carried out in a good hood, and it is advisable to use rubber gloves.

In a 5-l. flask surmounted by a water-cooled still head connected to a 30-in. spiral condenser set for downward distillation and connected to a well-cooled receiver (Note 1), 564 g. (4 moles) of β -aminoethylsulfuric acid (Note 2) is mixed with 1760 g. (1230 ml.) of 40% sodium hydroxide solution (704 g. of sodium hydroxide in 1056 ml. of water). The mixture is heated with a free flame until it just begins to boil. At this point external heating is discontinued (Note 3). The reaction that begins at the boiling point keeps the mixture boiling for several minutes. When this initial reaction has subsided, heating is resumed and about 500 ml. of distillate is collected as quickly as possible in the well-cooled receiver. To the chilled distillate 450–500 g. of potassium hydroxide pellets is added gradually, whereupon the imine separates as an upper layer. The organic layers from four such 4-mole runs are combined and left overnight in a refrigerator over about 400 g. of potassium hydroxide pellets. The aqueous layers are combined and distilled through a wrapped 10-in. Vigreux column attached to a 30-in. spiral condenser. The distillate boiling at 50–100° is chilled thoroughly, and 200–250 g. of potassium hydroxide pellets is added gradually. The upper layer of crude ethylenimine is separated and combined with the larger portion of base (Notes 4 and 5).

If an aqueous layer appears during drying of the combined organic layers, the upper layer (about 575–600 g.) is again separated, 200 g. of potassium hydroxide pellets is added, and the whole is distilled through the same apparatus as that used for distilling the aqueous portion. If no layer appears, the base is decanted from the hydroxide and distilled from a fresh 200-g. portion of potassium hydroxide. The fraction boiling at 50–100° (about 350 g.) is collected and dried over 100 g. of potassium hydroxide pellets.

The crude ethylenimine is separated and dried over fresh 100-g. portions of potassium hydroxide until an aqueous layer no longer appears (Note 6). It is then decanted from the drying agent and redistilled from 100 g. of potassium hydroxide.

The yield of ethylenimine (b.p. 56–58°) is 235–250 g. (34–37%). A stick of sodium hydroxide is added to act as a preservative, and the material is best stored in sealed bottles in a refrigerator (Notes 7, 8, and 9).

2. Notes

1. Cooling the receiver in a freezing mixture will cut the loss of the distillate to a minimum.

2. β -Aminoethylsulfuric acid of excellent quality is available from the B. F. Goodrich Company.

3. It is well to have an ice bath available to control the exothermic reaction, which may become quite violent.

4. The use of an efficient distilling column is recommended because the crude base contains higher-boiling by-products. One of these is the dimer, *N*- β -aminoethylethylenimine; b.p. 126–127.5°.

5. It has been suggested that the portion of ethylenimine, boiling at 50–100°, might be collected directly on distillation without separating the organic layer from the aqueous potassium hydroxide layer. This is not advisable, because heating ethylenimine in the presence of a base appears to increase polymerization. The quantity of the organic base contained in the concentrated aqueous solution of potassium hydroxide is sufficient, however, to warrant this distillation of the aqueous layer.

6. If the original separation is done carefully and if sufficient potassium hydroxide is used, an aqueous layer will separate during the first drying only. Should this not be the case, it may be worth while to combine all aqueous portions obtained and redistill them to obtain any material boiling at 50–100°.

7. Yields of 26.5% and 32% of ethylenimine have been reported.^{1,2}

8. Ethylenimine is strongly caustic and burns the skin. Inhalation of the vapor causes acute inflammation of the eyes, nose, and throat, with symptoms resembling those of bronchitis. After two or three days, the irritation subsides and the tissues return to normal, without suffering any apparent permanent injury. Continued exposure to the vapor may cause an individual to acquire an extreme sensitivity to it. Ethylenimine is also very inflammable and polymerizes with explosive violence under certain conditions.^{3,4}

9. Redistillation over fresh potassium hydroxide of the residue from this final distillation gives an additional 10–15 g. of ethylenimine, boiling at 56–58°. This redistillation is advisable when the residues from three to four 16-mole batches are combined.

3. Methods of Preparation

Ethylenimine has been prepared from β -bromoethylamine hydrobromide by reaction with silver oxide,⁵ potassium hydroxide,⁶ or sodium methoxide;⁷ from β -chloroethylamine hydrochloride by reaction with sodium methoxide⁷ or sodium hydroxide;⁸ and from β -aminoethylsulfuric acid by reaction with sodium hydroxide.^{1,2,3,9}

¹ Wenker, *J. Am. Chem. Soc.*, **57**, 2328 (1935).

² Jones, Langsjoen, Neumann, and Zomlefer, *J. Org. Chem.*, **9**, 125 (1944).

³ Mills and Bogert, *J. Am. Chem. Soc.*, **62**, 1177 (1940).

⁴ Pingree, *Am. Dyestuff Repr.*, **35**, 124 (1946).

⁵ Gabriel, *Ber.*, **21**, 1049 (1888).

⁶ Gabriel, *Ber.*, **21**, 2665 (1888); Gabriel and Stelzner, *Ber.*, **28**, 2929 (1895).

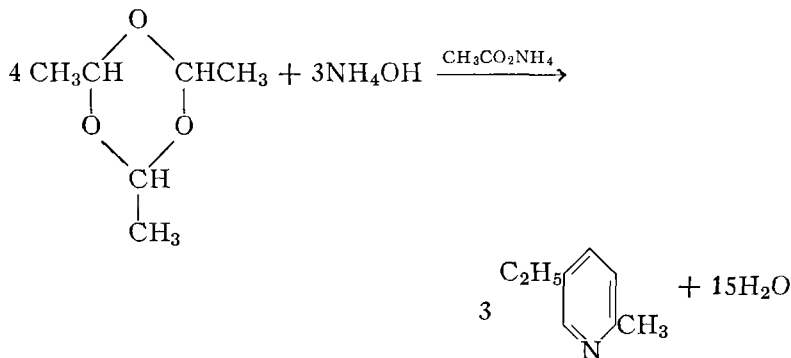
⁷ Knorr and Meyer, *Ber.*, **38**, 3130 (1905).

⁸ U. S. pat. 2,212,146 [*C. A.*, **35**, 463 (1941)].

⁹ Brit. pat. 460,888 [*C. A.*, **31**, 4676 (1937)].

5-ETHYL-2-METHYLPYRIDINE

(Pyridine, 5-ethyl-2-methyl-)



Submitted by ROBERT L. FRANK, FREDERICK J. PILGRIM, and
EDWARD F. RIENER.¹

Checked by R. S. SCHREIBER and T. L. ALDERSON.

1. Procedure

Two hundred and sixty-seven grams (296 ml., 4.38 moles) of 28% aqueous ammonium hydroxide, 207.5 g. (209 ml., 1.57 moles) of paraldehyde, and 5.0 g. (0.065 mole) of ammonium acetate are heated to 230° with continuous agitation in a 2-l. steel reaction vessel (Note 1), and the temperature is maintained at 230° for 1 hour (Note 2). The autoclave is then allowed to cool, and the two layers of the reaction mixture are separated (Note 3). To the non-aqueous layer is added 60 ml. of chloroform, causing separation of water which is combined with the aqueous layer. The aqueous layer is extracted with three 50-ml. portions of chloroform, and the extracts are combined with the main portion of the chloroform solution. After removal of the chloroform by distillation at atmospheric pressure, fractional distillation under reduced pressure through a 30-cm. Fenske-type column² gives a fore-run of water, paraldehyde, and α -picoline, b.p. 40–60°/17

mm., followed by 72-76 g. (50-53%) of 5-ethyl-2-methylpyridine, b.p. 65-66°/17 mm.; n_D^{20} 1.4971 (Note 4).

2. Notes

1. A steel reaction vessel of the type used for high-pressure catalytic hydrogenations is satisfactory. The pressure of the reaction mixture ranges from 800 to 3000 lb. A larger volume of reactants should not be used in a 2-l. reaction vessel.

2. The reaction is exothermic and in some reaction vessels may cause the temperature to rise above 230° for a short period. This has no apparent effect on the yield of product. The temperature measured is that of a thermocouple inserted in a well in the cover of the autoclave and corresponds to about 250° if the thermocouple is in the wall of the autoclave.

3. The mixture contains a small amount of solid material, apparently due to slight corrosion of the steel reaction vessel. If the solid causes the formation of an emulsion, it can be removed by filtration.

4. The yield may be increased to 60-70% by use of an 8:1 molar ratio of ammonium hydroxide to paraldehyde, but this is generally inconvenient because of the greatly increased volume of the reaction mixture.

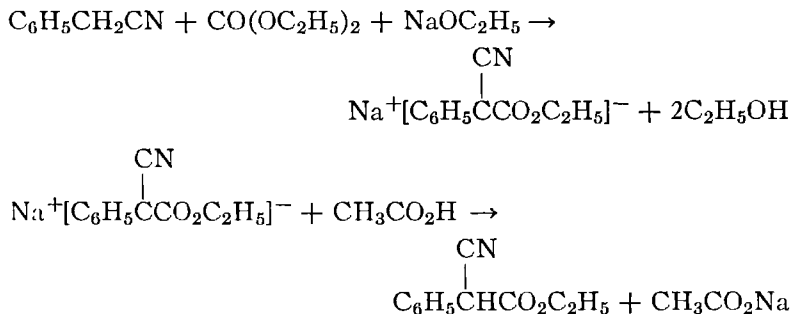
3. Methods of Preparation

5-Ethyl-3-methylpyridine (also known as "aldehyde-collidine") has been prepared by heating aldehyde-ammonia;³ aldehyde-ammonia and acetaldehyde^{4,5,6} or paraldehyde;^{6,7,8} aldol-ammonia and ammonia;⁹ paraldehyde and ammonia;^{10,11,12} acetamide,¹³ or acetamide and phosphorus pentoxide;¹⁴ ethylene glycol and ammonium chloride;¹⁵ ethylidene chloride^{16,17} or bromide¹⁸ and ammonia; ethylidene chloride and acetamide, ethylamine, or *n*-amylamine;¹⁵ crotonic acid and a calcium chloride-ammonia complex;¹⁹ and by passage of acetylene²⁰ or acetaldehyde²¹ and ammonia over alumina and other catalysts.

- ¹ Work done under contract with the Office of Rubber Reserve.
² Fenske, Tongberg, and Quiggle, *Ind. Eng. Chem.*, **26**, 1169 (1934).
³ Ador and Bacyer, *Ann.*, **155**, 297 (1870).
⁴ Dürkopf and Schlaugk, *Ber.*, **21**, 294 (1888).
⁵ Dürkopf, *Ber.*, **20**, 444 (1887).
⁶ Tschitschibabin and Oparina, *J. prakt. Chem.*, [2] **107**, 138 (1924).
⁷ Plath, *Ber.*, **21**, 3086 (1888).
⁸ Ladenburg, *Ann.*, **247**, 42 (1888).
⁹ Wurtz, *Ber.*, **8**, 1196 (1875).
¹⁰ Farbwerke vorm. Meister, Lucius and Brüning, Brit. pat. 146,869 [*C. A.*, **14**, 3675 (1920)]; Austrian pat. 81,299 [*Chem. Zentr.*, **92** II, 35 (1921)]; French pat. 521,891 [*Chem. Zentr.*, **92** IV, 805 (1921)].
¹¹ Graf and Langer, *J. prakt. Chem.*, **150**, 153 (1938).
¹² Frank, Blegen, Dearborn, Myers, and Woodward, *J. Am. Chem. Soc.*, **68**, 1368 (1946).
¹³ Pictet and Stchelin, *Compt. rend.*, **162**, 877 (1916).
¹⁴ Hesekei, *Ber.*, **18**, 3095 (1885).
¹⁵ Hofmann, *Ber.*, **17**, 1905 (1884).
¹⁶ Kraemer, *Ber.*, **3**, 262 (1870).
¹⁷ Dürkopf, *Ber.*, **18**, 920 (1885).
¹⁸ Tawildarow, *Ann.*, **176**, 15 (1875).
¹⁹ Fichter and Labhardt, *Ber.*, **42**, 4714 (1909).
²⁰ Tschitschibabin and Moschkin, *J. Russ. Phys. Chem. Soc.*, **54**, 611 (1922-1923); *J. prakt. Chem.*, [2] **107**, 109 (1924).
²¹ Tschitschibabin, Moschkin, and Tjaschelowa, *J. prakt. Chem.*, [2] **107**, 132 (1924).

ETHYL PHENYLCYANOACETATE

(Acetic acid, cyanophenyl-, ethyl ester)



Submitted by E. C. HORNING and A. F. FINELLI.

Checked by WILLIAM S. JOHNSON and H. WYNBERG.

1. Procedure

Sodium ethoxide is prepared from 12.0 g. (0.52 gram atom) of sodium and 300 ml. of anhydrous ethanol in a 1-l. three-necked round-bottomed flask fitted with a reflux condenser carrying a calcium chloride tube. After the sodium has dissolved completely, the condenser is arranged for distillation under reduced pressure and the excess ethanol is removed by heating the flask on a steam bath while the system is maintained at the pressure obtained with an ordinary aspirator (Note 1).

As rapidly as possible, after removal of the ethanol, the flask is fitted with a rubber-sealed stirrer, a dropping funnel, a distilling head containing a thermometer, and a condenser arranged for distillation into a flask protected by a calcium chloride tube. There are then added 300 ml. of dry diethyl carbonate, 80 ml. of dry toluene, and 58.5 g. (0.50 mole) of phenylacetonitrile (Note 2). The flask is heated, with good stirring, and the cake of sodium ethoxide soon dissolves. When distillation has started, dry toluene is added dropwise at about the same rate that the distillate is collected. Approximately 200–250 ml. of toluene should be added in a period of 2 hours (Note 3) while stirring and distillation are continued.

The mixture is cooled and transferred to a 1-l. beaker. After addition of 300 ml. of cold water, the aqueous phase is acidified with 35–40 ml. of acetic acid. The layers are separated and the water solution is extracted with three 75-ml. portions of ether. The organic solutions are combined, washed with 100 ml. of water, and dried over anhydrous magnesium sulfate. The low-boiling solvents are removed by distillation at atmospheric pressure, and the residue is distilled under reduced pressure through a short (15-cm.) Vigreux column. After a 1–5 g. forerun, the product is collected at 125–135°/3–5 mm. (Note 4). The yield is 66–74 g. (70–78%).

2. Notes

1. The success of this procedure is dependent upon the quality of the sodium ethoxide. The ethanol should be dried before use,¹ and the sodium ethoxide should not be heated to a temperature higher than 90-100°. The dry material can be transferred, but in this case it is advisable to prepare it in the flask in which it is to be used.

2. Commercial phenylacetonitrile should be distilled before use. The diethyl carbonate and toluene are dried by distillation.

3. Any ethanol remaining in the sodium ethoxide, together with the ethanol produced during the reaction, is removed during this period. The progress of the carbethoxylation reaction can be followed by temperature readings. During the first half of the heating period distillation usually occurs at a vapor temperature of 80-85°, but as the reaction nears completion and the ethanol is removed, the temperature rises to 110-115°. Near the end of the period, the sodium salt of ethyl phenylcyanoacetate appears as a precipitate.

4. Other observed boiling points are 129-131°/3 mm., 145-150°/7-8 mm. The product is a colorless liquid, n_D^{25} 1.5012-1.5019.

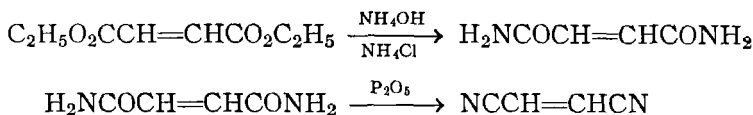
3. Methods of Preparation

This procedure is a modification of the method of Wallingford, Jones, and Homeyer.² The carbethoxylation of phenylacetonitrile is the only method of preparative value for this compound.

¹ *Org. Syntheses* Coll. Vol. 2, 155 (1943).

² Wallingford, Jones, and Homeyer, *J. Am. Chem. Soc.*, **64**, 576 (1942).

FUMARONITRILE



Submitted by DAVID T. MOWRY and JOHN MANN BUTLER.
 Checked by CHARLES C. PRICE and RICHARD D. GILBERT.

1. Procedure

Caution! Fumaronitrile is both vesicant and lachrymatory.

A. *Fumaramide*. A mixture of 516 g. (3.0 moles) of diethyl fumarate (Notes 1 and 2), 600 ml. of concentrated ammonium hydroxide (28%, sp. gr. 0.90, 9.0 moles), and 60 g. of ammonium chloride is placed in a 2-l. flask equipped with a stirrer and a thermometer. The reaction mixture is stirred at 25–30° with slight cooling for 7 hours (Note 3). The thick slurry of fumaramide is then filtered with suction, reslurried with 1 l. of water, filtered, and washed with about 50 ml. of ethanol. The white crystalline product is then dried in air or in an oven below 75° (Note 4). The yield is 270–300 g. (80–88%).

B. *Fumaronitrile*. The dry, finely powdered amide (Note 5) (228 g., 2.0 moles) and 613 g. (4.3 moles) of phosphorus pentoxide are placed in a 3-l. flask and thoroughly mixed by shaking. The flask is connected to a 1-l. suction flask receiver by means of a short 17-mm. i.d. 60° elbow extending about 15 cm. into the receiver. The receiver is cooled by immersion in an ice bath or by cold running water. The system is evacuated to 15–30 mm. by means of a water aspirator. The flask is then heated with one or two burners, using large soft flames. Heating should be started at the side, and moved toward the bottom as the reaction progresses (Note 6). The reaction mass froths and blackens, and the product distills and sublimes into the receiver. The elbow leading to the receiver must be heated occasionally to melt condensed fumaronitrile. Heating is continued until no more fu-

maronitrile distills from the reaction flask (1.5 to 2 hours) (Note 7). The product, usually white and sufficiently pure (m.p. 93–95°) for most purposes, is obtained in a yield of 125–132 g. (80–85%). The product is recrystallized conveniently (in a fume hood) by dissolving it in 150 ml. of hot benzene and decanting or filtering the solution into 500 ml. of hexane or petroleum ether (Notes 8 and 9). The yield of long, glistening prisms, m.p. 96°, amounts to 117–125 g. (75–80%).

2. Notes

1. Diethyl fumarate liquid and vapors often cause reddening and itching of the skin, which usually disappear after a few hours.

2. Dimethyl fumarate gives equally good results but is less convenient to handle because it is a solid.

3. Additional ammonium hydroxide may be added if the slurry becomes too thick.

4. Temperatures higher than 75° often cause yellowing of the amide and excessive foaming during the dehydration with phosphorus pentoxide.

5. The amide is considered sufficiently dry if no heat is evolved when a sample is shaken vigorously in a test tube with phosphorus pentoxide powder.

6. On somewhat smaller runs it may be more convenient to effect heating by the use of a wax or Wood's metal bath or an electric mantle. A bath or mantle temperature of 200° is sufficient for optimum yield. The reaction may froth vigorously if heated too rapidly or if the fumaramide is impure.

7. The cooled reaction flasks are easily cleaned by first soaking overnight in water and then rinsing with dilute sodium hydroxide solution.

8. *Caution!* This should be done in a hood. Fumaronitrile vapors and dust are irritating to the mucous membranes and are both vesicant and lachrymatory. In the event of skin contact, the area should be washed promptly and thoroughly with soap and water to avoid irritation and blistering.

9. The principal impurities are a benzene-insoluble brown tar and hexane-soluble ethyl β -cyanoacrylate.

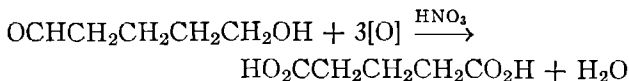
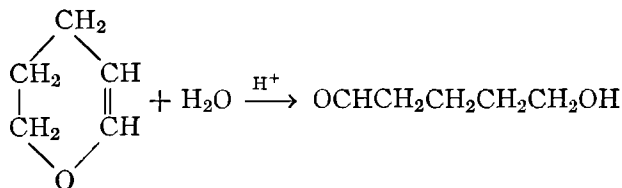
3. Methods of Preparation

The preparation described is based on the method of de Wolf and van de Straete.¹ Fumaronitrile has also been prepared by the reaction of diiodoethylene with cuprous cyanide.²

¹ deWolf and van de Straete, *Bull. classe sci., Acad. roy. Belg.*, **21**, 216 (1935) [*C. A.*, **29**, 3985 (1935)].

² Jennen, *Bull. classe sci., Acad. roy. Belg.*, **22**, 1169 (1936) [*C. A.*, **31**, 1010 (1937)].

GLUTARIC ACID



Submitted by J. ENGLISH, JR., and J. E. DAYAN.

Checked by ARTHUR C. COPE and MARK R. KINTER.

1. Procedure

In a 1-l. round-bottomed flask equipped with a reflux condenser are placed 400 ml. of 0.2 *N* nitric acid (5 ml. of concentrated nitric acid, sp. gr. 1.42, and 395 ml. of water) and 168.3 g. (2 moles) of dihydropyran (Note 1). The mixture is heated on a steam bath or a boiling water bath; the yellowish upper layer dissolves suddenly after 25 to 45 minutes of heating. The flask is swirled to aid the dissolution at this time, and the period of heating is extended for an additional 5 to 10 minutes.

While the hydrolysis of the dihydropyran is taking place, 800 g. (575 ml., 9.25 moles) of concentrated nitric acid (sp. gr. 1.42) is placed in a 2-l. three-necked flask and cooled in an ice-salt bath in a well-ventilated hood. The flask should be equipped with an efficient stirrer, separatory funnel, reflux condenser, and a thermometer. When the temperature of the solution reaches 0° , 5.75 g. of sodium nitrite is added and stirring is continued until most of it has dissolved; the solution becomes yellow.

The solution obtained by the hydrolysis of dihydropyran is placed in the separatory funnel, and about 10 ml. is added to the nitric acid solution at a temperature below 0° . After the evolution of brown nitrogen dioxide fumes begins (in about 10 minutes), the addition is continued at a rate that allows the temperature to be held below 10° (Note 2). The addition requires about 3 hours (Notes 3 and 4). When the addition is completed, the blue-green solution is stirred for an additional 90 minutes as brown fumes continue to be evolved. The cooling bath then is removed and stirring is continued as the temperature is allowed to rise slowly to $25-30^{\circ}$ (Note 5). As the reaction nears completion, the color changes from blue-green to green to light yellow. Appearance of the light yellow color indicates the end of the reaction and normally requires 2 to 3 hours after the addition is completed. The volume of the solution then is reduced either by evaporation on a steam bath or by distillation under reduced pressure.

In the latter method, after removal of all the water, an additional 100 ml. of water is added and the distillation is repeated to remove the remaining nitric acid. The solid residue remaining from either method of removing water from the reaction mixture is recrystallized from a mixture of 100 ml. of ether and 1 l. of benzene. Insoluble sodium nitrate and succinic acid are removed by filtration of the hot solution. Upon cooling, 185–198 g. (70–75%) of glutaric acid is obtained in the first crop, m.p. $89.5-91.5^{\circ}$ (Note 6). On concentrating the benzene solution to 200 ml. and cooling, an additional 18–23 g. of crude glutaric acid can be obtained (Note 7).

2. Notes

1. Dihydropyran is available from the Electrochemicals Department, E. I. du Pont de Nemours and Company, or can be prepared by the dehydration of tetrahydrofurfuryl alcohol.¹

2. More efficient cooling may shorten the time required for the addition.

3. As the hydrolyzed dihydropyran solution cools, it may become cloudy and δ -hydroxyvaleraldehyde may separate as a red liquid. The separation can be avoided by continuing to heat most of the solution while a small part is left in the separatory funnel, but it is not essential, for the yield is not affected by the separation of phases at this point. Oxidation of the pure aldehyde in a similar manner is stated to give a 90% yield of glutaric acid.²

4. The separatory funnel is removed after the addition is completed to facilitate the removal of nitrogen oxides.

5. Care should be taken that the temperature does not rise above room temperature; if this occurs much succinic acid is produced. If the temperature rises too high the cooling bath should be replaced again until the temperature does not exceed 25–30° on its removal.

6. The glutaric acid obtained has a neutralization equivalent of 66.3 (theory 66.1) and is suitable for most synthetic work.

7. This material melts at 80–82° and can be purified by recrystallization. In a series of preparations it is advantageous to save these residues and combine them for recrystallization.

3. Methods of Preparation

Other methods of preparation are cited in previous procedures for preparing glutaric acid in *Organic Syntheses*.³

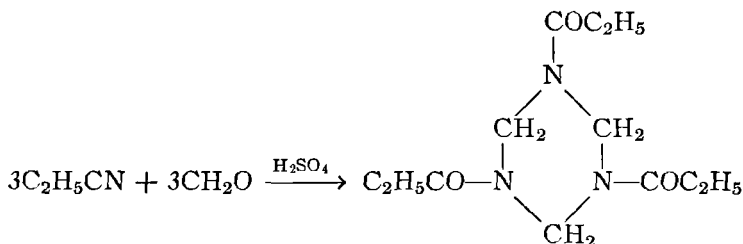
¹ Schniepp and Geller, *J. Am. Chem. Soc.*, **68**, 1646 (1946); *Org. Syntheses*, **23**, 25 (1943).

² U. S. pat. 2,389,950 [*C. A.*, **40**, 1539 (1940)].

³ *Org. Syntheses Coll. Vol. 1*, 289 (1943).

HEXAHYDRO-1,3,5-TRIPROPIONYL-*s*-TRIAZINE

(s-Triazine, hexahydro-1,3,5-tripropionyl)



Submitted by W. O. TEETERS and M. A. GRADSTEN.
 Checked by ARTHUR C. COPE and MARK R. KINTER.

1. Procedure

In a 3-l. three-necked flask equipped with a mechanical stirrer, a dropping funnel, a reflux condenser, and a thermometer are placed 110 g. (138 ml., 2 moles) of propionitrile (Note 1) and 8 g. (4.35 ml.) of concentrated sulfuric acid (sp. gr. 1.84). To the stirred mixture, which is heated to 90°, is added gradually a solution of 60 g. of trioxane (equivalent to 2 moles of formaldehyde) in 110 g. (138 ml., 2 moles) of propionitrile. During the addition the temperature of the reaction mixture is kept between 95° and 105° (Note 2). When the addition is complete (30 to 60 minutes) (Note 3) the reaction mixture is heated under reflux for an additional 3 hours, the internal temperature being kept at approximately 105°. The mixture is then allowed to cool to room temperature; during the cooling period the product crystallizes. The light-brown crystals are collected by filtration with suction on a Büchner funnel (Note 4). The solid (160 to 170 g.) is washed three times with 100-ml. portions of ether and air-dried. The crude yellow product (130 to 135 g., melting point between 164° and 170°) is recrystallized from 160 ml. of 90% ethanol. The product is collected on a Büchner funnel, washed on the funnel with 100 ml. of ether, and air-dried. In this way 105 to 115 g.

(62 to 68%) of white crystals of hexahydro-1,3,5-tripropionyl-*s*-triazine melting at 170–172° is obtained (Note 5). Recrystallization from 95% ethanol (2.4 ml. per g.) results in 91% recovery of an analytically pure product, m.p. 173.2–174.1° (cor.).

2. Notes

1. A practical grade of propionitrile obtained from the Eastman Kodak Company was used.

2. During the addition external heating may be discontinued and the internal temperature regulated by the rate of addition.

3. The reaction mixture turns from light yellow to a reddish brown color during the addition.

4. An appreciable amount of propionitrile (100 to 110 g.) can be recovered from the filtrate. If subsequent batches of hexahydro-1,3,5-tripropionyl-*s*-triazine are being prepared the filtrate can be added to the next charge without isolating the propionitrile. To counteract the accumulation of impurities, activated carbon may be used in the recrystallization of the reaction product.

5. Another 35 to 50 g. of a less pure product (m.p. 160–165°) may be isolated by concentrating the mother liquor.

3. Methods of Preparation

A hexahydro-1,3,5-triacetyl-*s*-triazine was first prepared by Duden and Scharff¹ from ammonium chloride, formalin, and benzoyl chloride or from hexamethylenetetramine and benzoyl chloride. A procedure similar to the one described² also has been used for the preparation of hexahydro-1,3,5-triacetyl-, tri(β -chloropropionyl)-, triacrylyl-, trimethacrylyl-, and tribenzoyl-*s*-triazine. Several of these compounds also have been prepared by Wegler and Ballauf³ from the corresponding nitriles and paraformaldehyde in the presence of acetic anhydride and sulfuric acid.

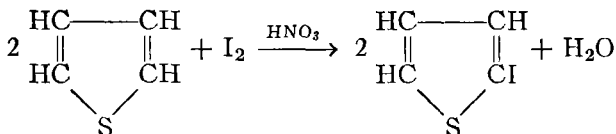
¹ Duden and Scharff, *Ann.*, **288**, 247 (1895).

² Gradsten and Pollock, *J. Am. Chem. Soc.*, **70**, 3079 (1948).

³ Wegler and Ballauf, *Chem. Ber.*, **81**, 527 (1948).

2-iodothiophene

(Thiophene, 2-iodo-)



Submitted by HENRY Y. LEW and C. R. NOLLER.

Checked by CLIFF S. HAMILTON and FRANK A. BOWER.

1. Procedure

In a 200-ml. three-necked flask fitted with a mechanical stirrer (Note 1), a reflux condenser, and a separatory funnel, and set up in a hood, are placed 38 g. (0.15 mole) of iodine and 42 g. (39 ml., 0.50 mole) of thiophene (Note 2). A solution of 28 ml. (0.44 mole) of nitric acid (sp. gr. 1.42) diluted with an equal volume of water is placed in the separatory funnel, from which approximately one-fourth of the nitric acid is added slowly and with vigorous stirring. Slight heating may be necessary to start the reaction, but once initiated it proceeds vigorously with the evolution of brown oxides of nitrogen. Cooling with an ice bath may be necessary to control the reaction. After the evolution of gases has subsided, the remaining nitric acid is added dropwise, and the reaction proceeds smoothly at room temperature with continual evolution of oxides of nitrogen. After all the nitric acid has been added, the solution is heated under reflux on a water bath for 30 minutes.

The reaction mixture is allowed to stand, and the red organic layer is separated, mixed with 40 ml. of 10% sodium hydroxide solution, and steam-distilled (Note 3). The yellow oil is separated, dried over anhydrous calcium chloride, and distilled at reduced pressure from a modified Claisen flask. The yield is 43-45 g. (68-72%); b.p. 89-93°/36 mm.; n_D^{25} 1.6465.

2. Notes

1. The seal for the mechanical stirrer used (Fig. 2) is made from two one-hole rubber stoppers and a piece of glass tubing with glycerin as a seal and lubricant. According to the submitters, it is better than a mercury seal, not only for reactions where halogens, halogen acids, or compounds that react with mercury are present, but also for practically any other reaction

since the handling of mercury always requires a considerable amount of care.

The glass tubing *D*, about 10 cm. in length, is just large enough in diameter to permit the stirrer *E* to rotate freely. The smaller of the two one-hole rubber stoppers, *A*, is bored to a depth of about 7 mm. with a cork-borer whose diameter is approximately 3 mm. larger than that of tubing *D*, and then this section is cut out with a pair of scissors. Rubber stopper *B* is 10–15 mm. larger in diameter than *A*. When assembled, tubing *D* fits tightly in rubber stopper *B*, and protrudes out at the top about 4 mm., and rubber stopper *A* fits

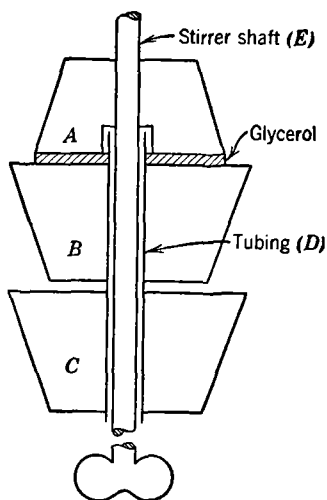


FIG. 2. Seal for a mechanical stirrer made from rubber stoppers and glass tubing using glycerol as a seal and lubricant.

tightly about stirrer *E* and rests on top of rubber stopper *B*. Glycerol is used as a seal and as a lubricant between the contact surfaces of rubber stoppers *A* and *B*, and the portion of tubing *D* protruding out of rubber stopper *B* acts as a wall in preventing glycerol from flowing down inside the tubing. When the stirrer motor is on, rubber stopper *A* rotates with stirrer *E*. Rubber stopper *C* fits tightly over tubing *D* and in the mouth of the reaction flask.

2. When the preparation is carried out in larger quantities, evolution of heat accompanies the mixing of iodine and thio-

phene, and unless the mixture is stirred well, it will solidify into a hard mass. By keeping the quantities reasonably small, this tendency to solidify is reduced to a minimum.

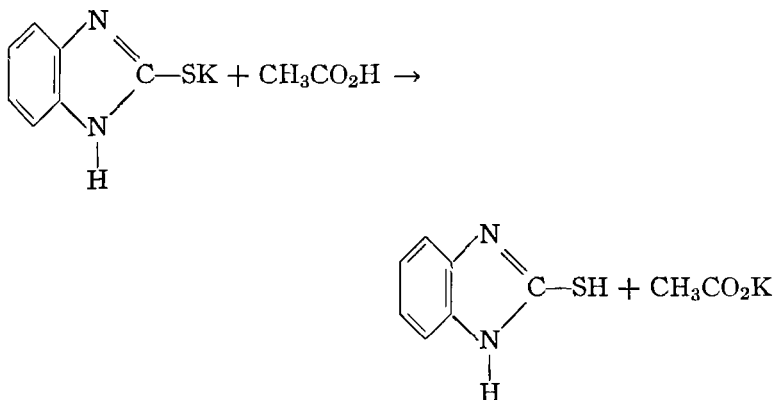
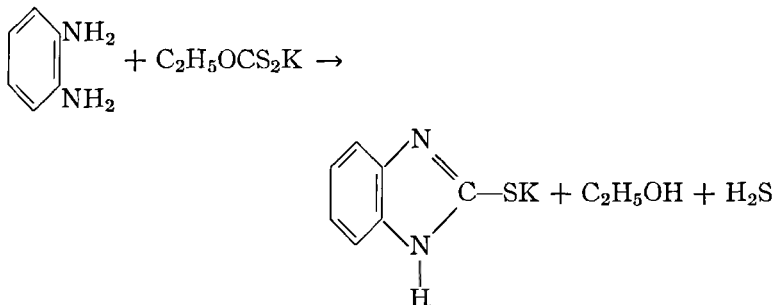
3. Toward the end of the distillation a small amount (0.5–2.0 g.) of 2-iodo-5-nitrothiophene is collected in the condenser and the receiver. The amount formed increases with increase in the temperature of the reaction mixture.

3. Method of Preparation

2-Iodothiophene has been prepared by the action of iodine and mercuric oxide on thiophene.¹

¹ Meyer and Kreis, *Ber.*, **17**, 1558 (1884); Thyssen, *J. prakt. Chem.*, [2] **65**, 5 (1902); *Org. Syntheses* Coll. Vol. **2**, 357 (1943).

2-MERCAPTOBENZIMIDAZOLE

(2-Benzimidazolethiol)¹

Submitted by J. A. VAN ALLAN and B. D. DEACON.

Checked by CLIFF S. HAMILTON and YAO-HUA WU.

1. Procedure

A mixture of 32.4 g. (0.3 mole) of *o*-phenylenediamine,² 52.8 g. (0.33 mole) of potassium ethyl xanthate (Note 1), 300 ml. of 95% ethanol, and 45 ml. of water in a 1-l. flask is heated under reflux for 3 hours. Norit (12 g.) is then added cautiously, and after the mixture has been heated at the reflux temperature for 10 minutes the Norit is removed by filtration. The filtrate is heated to 60–70°, 300 ml. of warm tap water (60–70°) is added, and then 25

ml. of acetic acid in 50 ml. of water is added with good stirring. The product separates as glistening white crystals, and the mixture is placed in a refrigerator for 3 hours to complete the crystallization. The product is collected on a Büchner funnel and dried overnight at 40°. The yield is 37.8-39 g. (84-86.5%) of 2-mercaptobenzimidazole melting at 303-304° (cor.) (Notes 2 and 3).

2. Notes

1. The potassium ethyl xanthate may be replaced by 19 g. of potassium hydroxide and 26 g. (21 ml., 0.34 mole) of carbon disulfide. The yield and quality of the product are the same.

2. The quality of the product is excellent. Recrystallization may be effected from 95% ethanol as a solvent. Recovery is about 90%; there is no change in the melting point.

3. 2-Mercaptobenzoxazole, m.p. 193-195°, can be prepared in 80% yield by a similar procedure, using *o*-aminophenol in place of *o*-phenylenediamine.

3. Methods of Preparation

2-Mercaptobenzimidazole has also been prepared from *o*-phenylenediamine by heating the thiocyanate to 120-130°;³ by heating with aqueous potassium thiocyanate (in which case 2-aminophenylthiourea is a by-product);⁴ by the action of thiophosgene in chloroform;⁵ by heating with carbon disulfide in alcohol⁶ or in water;⁷ and by heating the hydrochloride with thiourea to 170-180°.⁸

¹ Before 1937 the *Chemical Abstracts* name was 2-benzimidazole mercaptan. Other names found in the literature are *o*-phenylenethiourea and 2-thiobenzimidazolone.

² *Org. Syntheses* Coll. Vol. **2**, 501 (1943).

³ Lellmann, *Ann.*, **221**, 9 (1883).

⁴ Frerichs and Hupka, *Arch. Pharm.*, **241**, 165 (1903).

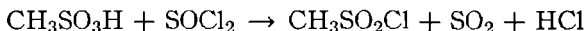
⁵ Billeter and Steiner, *Ber.*, **20**, 231 (1887).

⁶ Gucci, *Gazz. chim. ital.*, [1] **23**, 295 (1893).

⁷ Kawaoka, *J. Soc. Chem. Ind., Japan* **43**, Suppl. binding 223 (1940) [*C. A.*, **35**, 2368 (1941)].

⁸ Kym, *J. prakt. Chem.*, [2] **75**, 324 (1907).

METHANESULFONYL CHLORIDE



Submitted by PETER J. HEARST and C. R. NOLLER.

Checked by R. S. SCHREIBER, B. D. ASPERGREN, and R. V. HEINZELMANN.

1. Procedure

In a 1-l. three-necked flask fitted with a mechanical stirrer, a reflux condenser, a thermometer, and a separatory funnel (Note 1), and set up in a hood, is placed 152 g. (105 ml., 1.5 moles) of methanesulfonic acid (Note 2). The acid is heated to 95° on a steam bath, and 238 g. (146 ml., 2.0 moles) of thionyl chloride (Note 3) is added over a period of 4 hours. The temperature is kept at 95° throughout the addition and for 3.5 hours after it is completed.

The product is transferred to a modified Claisen flask (Note 4) and distilled under reduced pressure, heat being supplied by an oil bath (Note 5). Most of the thionyl chloride distills at room temperature. The yield of almost colorless product distilling at 64–66°/20 mm. (Note 6) is 122–143 g. (71–83%); n_D^{23} 1.451.

2. Notes

1. The checkers recommend the use of silicone grease on all glass joints.

2. The methanesulfonic acid is a commercial product supplied by the Standard Oil Company of Indiana and reported to be 95% pure and to contain 2% water.

3. Eastman Kodak Company thionyl chloride (b.p. 75–76°) was used without further purification.

4. The checkers used a Claisen head with an attached 10-cm. Vigreux column.

5. A free flame should be avoided, because local superheating causes charring and decomposition. The fumes from the decomposition cause the product (which normally is colorless) to darken.

The bath temperature should not exceed 115° at the end of the distillation.

6. The checkers observed a boiling point of 61–62°/18 mm.

3. Methods of Preparation

Methanesulfonyl chloride has been prepared by the chlorination of methyl thiocyanate,¹ S-methylthiourethan,² sodium methylthiosulfate³ or S-methylisothiuronium sulfate;⁴ from sodium methanesulfonate by the action of phosphorus pentachloride,^{5,6} phosphorus oxychloride,⁶ or benzotrichloride;⁷ from methanesulfonic acid by the action of phosphorus pentachloride;⁸ or by the reaction of methylmagnesium iodide with sulfuryl chloride.⁹

¹ Johnson and Douglass, *J. Am. Chem. Soc.*, **61**, 2548 (1939); Johnson, U. S. pat. 2,174,856 [*C. A.*, **34**, 778 (1940)].

² Battegay and Krebs, *Compt. rend.*, **206**, 1262 (1938).

³ Douglass and Johnson, *J. Am. Chem. Soc.*, **60**, 1486 (1938).

⁴ Johnson and Sprague, *J. Am. Chem. Soc.*, **58**, 1348 (1936).

⁵ Billeter, *Ber.*, **38**, 2019 (1905); Helferich and Gnüchtel, *Ber.*, **71**, 712 (1938).

⁶ Dutt, *J. Chem. Soc.*, **125**, 1463 (1924).

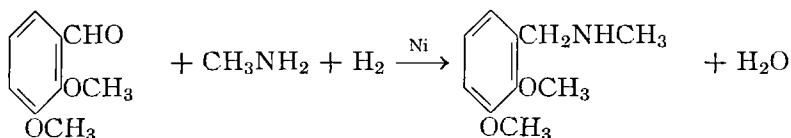
⁷ I. G. Farbenind., A.-G., Ger. pat. 574,836 [*C. A.*, **27**, 4543 (1933)].

⁸ Carius, *Ann.*, **114**, 142 (1860); Gowan, *J. prakt. Chem.*, [2] **30**, 281 (1884).

⁹ Cherbuliez and Schnauder, *Helv. Chim. Acta*, **6**, 256 (1923).

N-METHYL-2,3-DIMETHOXYBENZYLAMINE

(Benzylamine, 2,3-dimethoxy-N-methyl-)



Submitted by DON M. BALCOM and C. R. NOLLER.

Checked by HOMER ADKINS and WALTER W. GILBERT.

1. Procedure

To a solution of 41.6 g. (0.25 mole) of purified 2,3-dimethoxybenzaldehyde (Note 1) in 150 ml. of 95% ethanol is added 23.4 g. (0.75 mole) of methylamine in 50 to 75 ml. of water (Note 2). The mixture is heated to boiling and placed in a 500-ml. heavy-walled bottle (Note 3), and 6 g. of Raney nickel catalyst is added (Note 4). The bottle is connected to a low-pressure hydrogenation apparatus,¹ the system is flushed with hydrogen, and the mixture is shaken with hydrogen at an initial pressure of 45 lb. until 0.25 mole of hydrogen is absorbed and the absorption ceases (Note 5).

After the completion of the reduction the catalyst is removed by filtration and the alcohol is evaporated on the steam bath. To the resulting syrupy solution is added about 85 ml. of 3 *N* hydrochloric acid (sufficient to make the solution acid to Congo red paper). The solution is extracted with three 50-ml. portions of ether. The aqueous layer is made alkaline with 50 ml. of 6 *N* sodium hydroxide, and the amine layer is separated. The aqueous layer is extracted with three 50-ml. portions of ether, and the extracts are combined with the amine layer. The ether solution is dried overnight with solid potassium hydroxide and is filtered to remove suspended matter; the flask is rinsed with 25 ml. of ether. The ether is removed on a steam bath, and the amine is distilled under reduced pressure from a modified Claisen flask having a 15-cm. indented column. The *N*-methyl-2,3-dimethoxybenzylamine distils at 120-124°/8 mm. and is obtained in a yield of 39-42 g. (86-93%) (Notes 6 and 7).

2. Notes

1. The 2,3-dimethoxybenzaldehyde employed was a dark-colored product supplied by the Monsanto Chemical Company or Eastman Kodak Company. It was purified by distilling at reduced pressure and crystallizing from methanol, after which it was colorless and melted at 52-54°.

2. The submitters used 72 g. of a 33% water solution of methylamine; the checkers used 100 g. of a 23% solution.

3. The submitters used a pint hydrogenation bottle wound with 30 ft. of No. 24 Nichrome wire insulated with asbestos paper. Before the reaction the current was adjusted by means of a variable transformer so that the solution was maintained at approximately 70° during the reaction. The checkers used a 500-ml. centrifuge bottle without provision for heating.

4. The submitters used Raney nickel catalyst prepared as described by Mozingo.² The checkers used W-6 Raney nickel catalyst.³

5. The time required depends upon the activity of the catalyst and the temperature of reaction. The submitters reported that 90–95% of the calculated amount of hydrogen was taken up in 90 minutes at 70° whereas 20 hours was required at room temperature. The checkers found the reaction to be complete after 36 to 41 minutes, the temperature dropping during the period from 70° to 30° since no provision was made for heating. When the whole hydrogenation was carried out at room temperature the period of reaction was 90 minutes with the W-6 Raney nickel catalyst.

6. The submitters state that with a 1:1 mole ratio of aldehyde to amine the yield dropped to 75%, presumably because more of the aldehyde was reduced.

7. The submitters report that similar yields of methylaryl amines were obtained from benzaldehyde, anisaldehyde, veratraldehyde, and piperonal.

3. Methods of Preparation

N-Methyl-2,3-dimethoxybenzylamine has been prepared by the reaction of 2,3-dimethoxybenzyl chloride with methylamine⁴ and by the catalytic reduction of a mixture of 2,3-dimethoxybenzaldehyde and methylamine using Adams' platinum catalyst.⁵

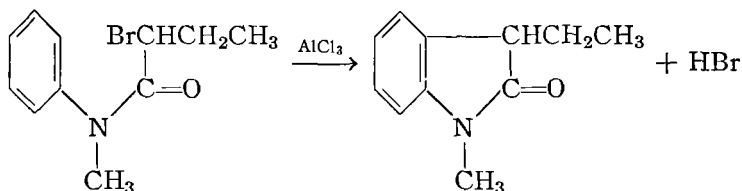
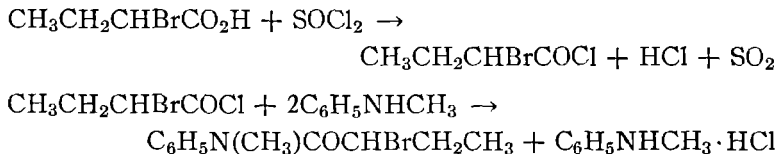
¹ *Org. Syntheses* Coll. Vol. 1, 61 (1941).

² *Org. Syntheses*, 21, 15 (1941).

³ Adkins and Billica, *J. Am. Chem. Soc.*, 70, 695 (1948); *Org. Syntheses*, 29, 24 (1949).

⁴ Douctteau, *Bull. soc. chim. France*, [4] 11, 655 (1912).

⁵ Sapp, dissertation, Stanford University, 1940.

1-METHYL-3-ETHYLOXINDOLE**(Oxindole, 3-ethyl-1-methyl)**

Submitted by M. W. RUTENBERG and E. C. HORNING.
 Checked by WILLIAM S. JOHNSON and C. A. ERICKSON.

1. Procedure

In a 500-ml. round-bottomed flask fitted with a calcium chloride drying tube are placed 226 g. (1.35 moles) of α -bromo-*n*-butyric acid (Note 1) and 284 g. (175 ml., 2.39 moles) of thionyl chloride (Note 2). A small piece of porous plate is added, and the reaction mixture is allowed to stand at room temperature for 48 hours (Note 3). The excess thionyl chloride is removed by distillation, and the acid chloride is collected at 147–153° (Note 4). The yield of colorless product is 168–197 g. (67–78%).

In a 1-l. three-necked flask fitted with a Hershberg wire stirrer, a reflux condenser equipped with a calcium chloride drying tube, and a dropping funnel, are placed 237 g. (2.21 moles) of methyl-aniline (Note 5) and 300 ml. of dry benzene (Note 6). Stirring is started, and the reaction mixture is cooled in an ice-water bath during the dropwise addition of 197 g. (1.06 moles) of α -bromo-*n*-butyryl chloride diluted with approximately 40 ml. of dry benzene. The addition requires approximately 1 hour, and the reaction mixture becomes thick owing to the separation of methyl-

aniline hydrochloride. The mixture is stirred for an additional 30 minutes and is then set aside protected by a calcium chloride tube for approximately 12 hours. The colorless methylaniline hydrochloride is removed by filtration with suction and washed with two 25-ml. portions of benzene. The combined filtrate and washings are washed with three 100-ml. portions of 5% hydrochloric acid to remove excess methylaniline, and then with two 100-ml. portions of water (Note 7). The benzene layer is dried over anhydrous magnesium sulfate. The drying agent is removed by filtration and the solvent is removed by distillation (the last traces of solvent are removed with an aspirator) to give N-methyl- α -bromo-*n*-butyranilide (Note 8).

The crude N-methyl- α -bromo-*n*-butyranilide is placed in a 500-ml. three-necked round-bottomed flask equipped with a Hershberg wire stirrer and a reflux condenser fitted with a calcium chloride drying tube. To the stirred liquid, cooled in an ice-water bath, is added 281 g. (2.1 moles) of aluminum chloride (reagent grade, powdered) in portions over a period of about 30 minutes (Note 9). A thermometer is then introduced, and the cooling bath is replaced by a source of heat (Note 10). The reaction commences at about 80° with the evolution of hydrogen bromide (Note 11) and becomes very vigorous at 95–105°. At this point, no external heat need be applied, because the heat of reaction carries the temperature to 110–115°. When the reaction slows down, the temperature is raised to 160–170°, and the dark mixture is then allowed to cool to about 80–90°. The reaction mixture is poured *cautiously* into a 3-l. beaker about one-fourth full of cracked ice. Additional ice is added as required. The last traces of product are removed from the flask with the aid of hydrochloric acid and ice. Concentrated hydrochloric acid (75 ml.) is added to aid the decomposition of the aluminum chloride complex. The brown oil is separated after adding 75 ml. of ether, and the aqueous layer is extracted with two 100-ml. portions of ether. The combined organic layers are washed with two 75-ml. portions of 5% hydrochloric acid, two 100-ml. portions of water, two 75-ml. portions of saturated sodium bicarbonate solution, and two 100-ml. portions of water. After drying over anhydrous mag-

nesium sulfate the ether is distilled, and the residue is distilled under reduced pressure. The main fraction is collected at 103–107°/0.5 mm. The yield is 126–131 g. (68–71% based on the acid chloride) of pale yellow 1-methyl-3-ethyloxindole, n_D^{25} 1.5569–1.5580.

2. Notes

1. The α -bromo-*n*-butyric acid obtained from the Eastman Kodak Company, which had a boiling range of 2°, proved to be satisfactory.

2. Commercial thionyl chloride was distilled before use.

3. The reaction mixture is allowed to stand under an efficient hood during this period. A yield of 166 g. of product may be obtained by refluxing the mixture for 2.5 hours in a 1-l. flask equipped with condenser and drying tube.

4. The submitters used apparatus fitted with ground-glass joints for this and subsequent operations.

5. Redistilled N-methylaniline was used, b.p. 195–196°.

6. The benzene was dried by distillation.

7. Sodium chloride was added to the hydrochloric acid solution and to the wash water to reduce emulsion formation.

8. The crude N-methyl- α -bromo-*n*-butyranilide may be used directly for the ring closure or, if desired, may be purified by distillation (b.p. 117–118°/0.4 mm., 125–127°/0.8 mm., 175–184°/24 mm.).

9. The aluminum chloride is introduced into the reaction mixture without exposure to the atmosphere.¹ The mixture becomes quite viscous, and a powerful stirrer is needed.

10. An electric heating jacket was found to be most satisfactory.

11. The reaction should be carried out under an efficient hood with provision for the absorption of evolved hydrogen bromide.

3. Methods of Preparation

This method is a general one for the preparation of oxindoles and 1-methyloxindoles, and is based on the procedure of Stollé² as developed by Julian and Pikel.³

1-Methyl-3-ethyloxindole has been prepared previously by methylation of 3-ethyloxindole with methyl iodide.⁴ It has also been made from 1-methyloxindole by acylation with ethyl acetate in the presence of sodium ethoxide, followed by hydrogenation over a palladium catalyst.⁵

¹ Fieser, *Experiments in Organic Chemistry*, 2nd ed., p. 311, D. C. Heath and Company, Boston, 1941.

² Stollé, *J. prakt. Chem.*, [2] **128**, 1 (1930).

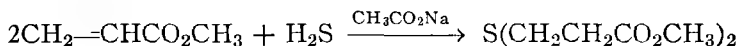
³ Julian and Pikel, *J. Am. Chem. Soc.*, **57**, 563 (1935). Cf. Porter, Robinson, and Wyler, *J. Chem. Soc.*, **1941**, 620.

⁴ Brunner, *Monatsh.*, **18**, 545 (1897).

⁵ Julian, Pikel, and Wantz, *J. Am. Chem. Soc.*, **57**, 2026 (1935).

METHYL β -THIODIPROPIONATE

(Propionic acid, β,β' -thiodi-, dimethyl ester)



Submitted by EDWARD A. FEHNEL and MARVIN CARMACK.

Checked by ARTHUR C. COPE and JAMES J. RYAN.

1. Procedure

Caution! This preparation should be conducted in a hood to avoid exposure to poisonous hydrogen sulfide.

A mixture of 150 g. (1.74 moles) of methyl acrylate (Note 1), 100 g. (0.73 mole) of sodium acetate trihydrate, and 800 ml. of 95% ethanol (Note 2) is placed in a 2-l. two-necked flask fitted with an efficient reflux condenser and a sintered-glass bubbler tube which reaches almost to the bottom of the flask. The mixture is heated on the steam bath until all the solid is dissolved and the solution is refluxing gently. A steady stream of hydrogen sulfide gas (Note 3) is introduced into the boiling solution through the bubbler tube while heating is continued for a period of 25 hours. The gas flow is then stopped, the condenser is changed for distillation, and the solvent, along with some unreacted methyl acrylate, is distilled from the mixture on the steam bath. About 200 ml. of ether and 400 ml. of water are added to the residue in

the flask, and after thorough agitation the layers are separated. The aqueous layer is washed with four 50-ml. portions of ether, and the washings are added to the original ether layer. The combined ether extracts are dried over anhydrous sodium sulfate, the ether is removed by distillation on the steam bath, and the residue is distilled under reduced pressure. Methyl β -thiodipropionate is obtained as a colorless oil, b.p. 162–164°/18 mm., 138–139°/6 mm.; n_D^{25} 1.4713. The yield is 128–145 g. (71–81%).

2. Notes

1. A good grade of commercial methyl acrylate containing hydroquinone is entirely satisfactory. Material of doubtful quality may be redistilled (into a receiver containing hydroquinone), b.p. 78–81°.

2. Either methanol or 95% ethanol may be used as the solvent. No ester interchange was observed to occur under the conditions employed.

3. Commercial tank hydrogen sulfide was used. The flow was regulated by passing the gas through a gas-washing bottle containing a little water. A rate of about 3–5 bubbles per second was maintained during the reaction.

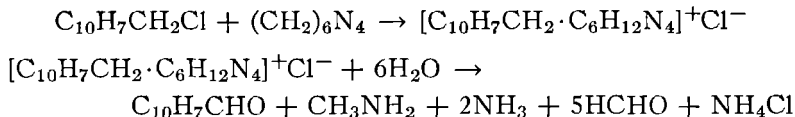
3. Methods of Preparation

β -Thiodipropionic acid esters have been prepared by the addition of hydrogen sulfide to the corresponding acrylic esters in the presence of basic catalysts with ¹ or without ² solvents. The ethyl ester has also been prepared by the treatment of ethyl β -chloropropionate with sodium sulfide.³

¹ I. G. Farbenind. A.-G., Fr. pat. 797,606 [*Chem. Zentr.*, **107** II, 1062 (1936)] [*C. A.*, **30**, 8244 (1936)]. Cf. also Ger. pat. 669,961 [*C. A.*, **33**, 5415 (1939)].

² Gershbein and Hurd, *J. Am. Chem. Soc.*, **69**, 241 (1947).

³ Arndt and Bekir, *Ber.*, **63**, 2393 (1930).

1-NAPHTHALDEHYDE

Submitted by S. J. ANGYAL, J. R. TETAZ, and J. G. WILSON.
 Checked by R. S. SCHREIBER and PAUL E. MARLATT.

1. Procedure

Caution! Precautions should be taken to avoid contact with 1-chloromethylnaphthalene, which is a lachrymator and a vesicant, and with the aldehyde, which seems to possess the same properties to a lesser degree.

In a 1-l. flask fitted with a reflux condenser are placed 106 g. (0.6 mole) of 1-chloromethylnaphthalene¹ (Note 1), 168 g. (1.2 moles) of hexamethylenetetramine, 250 ml. of glacial acetic acid, and 250 ml. of water. This mixture is heated under reflux for 2 hours. In about 15 minutes the solution becomes homogeneous, and then an oil starts to separate. After the reflux period, 200 ml. of concentrated hydrochloric acid is added and refluxing is continued for an additional 15 minutes (Note 2). After cooling, the mixture is extracted with 300 ml. of ether; the ether layer is washed three times with 100-ml. portions of water, then with 100 ml. of 10% sodium carbonate solution (Note 3), and again with 100 ml. of water. The ether extract is dried with about 15 g. of anhydrous sodium sulfate and filtered, and the ether is removed by distillation. The residual liquid is distilled under reduced pressure, the distillate being collected at 105–107°/0.2 mm. or 160–162°/18 mm. (Note 4). The yield of colorless 1-naphthaldehyde freezing between 0.0° and 2.5° (Note 5) is 70–77 g. (75–82%).

2. Notes

1. The chloromethylnaphthalene used melted at 24–26°. Material with a lower melting point can be used, but the yield is correspondingly smaller; e.g., a sample having a melting point of 15–18° gave a 73% yield of slightly impure 1-naphthaldehyde.

The checkers found that crude chloromethylnaphthalene obtained from the preparation in *Organic Syntheses*¹ could be used with good results. Naphthalene, paraformaldehyde, hydrochloric acid, and phosphoric acid are heated under reflux according to the procedure described. After the crude product is washed with water, 10% potassium carbonate, and water, it is dissolved directly in 500 ml. of glacial acetic acid, diluted with 500 ml. of water, and treated with hexamethylenetetramine by the procedure described above. The over-all yield of almost colorless 1-naphthaldehyde is 162 g., b.p. 162–164°/18 mm.; n_D^{25} 1.6503 (52% yield based on naphthalene).

In this variation of the preparation, it is best to use a wide-bore tube as a condenser to remove the unreacted naphthalene. After the naphthalene has been distilled, the wide-bore tube is replaced with an ordinary condenser and the naphthaldehyde is distilled in the usual manner.

2. The various amines and aldehydes present combine to form Schiff's bases. If these are not hydrolyzed by a strong acid, they will contaminate the final product.

3. Care should be exercised when washing the solution with sodium carbonate because some carbon dioxide is evolved.

4. The brown distillation residue contains some methylene- α -naphthylmethylamine.

5. The melting point of 1-naphthaldehyde given by Stephen² (33–34°) is apparently incorrect. A sample that was purified through the bisulfite addition compound and redistilled had a freezing point of 2.5°.

In no instance could the checkers obtain a completely colorless product even though it was redistilled several times with ordinary laboratory distilling apparatus.

3. Methods of Preparation

1-Naphthaldehyde has been prepared from calcium α -naphthoate by distillation with calcium formate;³ from α -naphthylcarbinol by oxidation with chromic acid;^{4,5} from α -naphthylglyoxylic acid by heating with aniline and hydrolyzing the anil;⁶ from α -naphthylmagnesium bromide and ethoxymethylethaneaniline^{7,8} or ethyl orthoformate.^{9,10} This Grignard reagent has also been converted to the dithioacid with carbon disulfide and the acid converted to 1-naphthaldehyde (through the semicarbazone).¹¹

1-Naphthaldehyde has been made from α -naphthonitrile by reduction with stannous chloride,^{2,12} and from naphthalene by the action of aluminum chloride, hydrogen cyanide, and hydrochloric acid.¹³ The best preparation is the Sommelet reaction¹⁴ from α -chloro- or α -bromomethylnaphthalene and hexamethylenetetramine in aqueous alcohol^{15,16,17,18,19} or glacial acetic acid.^{20,21} This method has been improved in the present procedure by the use of 50% acetic acid as solvent.

¹ *Org. Syntheses*, **24**, 30 (1944).

² Stephen, *J. Chem. Soc.*, **127**, 1877 (1925).

³ Lugli, *Gazz. chim. ital.*, **11**, 394 (1881).

⁴ Bamberger and Lodter, *Ber.*, **21**, 259 (1888).

⁵ Ziegler, *Ber.*, **54**, 739 (1921).

⁶ Rousset, *Bull. soc. chim. France*, [3] **17**, 303 (1897).

⁷ Monier-Williams, *J. Chem. Soc.*, **89**, 275 (1906).

⁸ Gattermann, *Ann.*, **393**, 227 (1912).

⁹ Bodroux, *Compt. rend.*, **138**, 701 (1904); *Bull. soc. chim. France*, [3] **31**, 587 (1904).

¹⁰ Kikkaji, *Biochem. Z.*, **35**, 67 (1911).

¹¹ Wuyts, Berman, and Lacourt, *Bull. soc. chim. Belg.*, **40**, 665 (1931).

¹² King, l'Ecuyer, and Openshaw, *J. Chem. Soc.*, **1936**, 353.

¹³ Kinkel, Ayling, and Beynon, *J. Chem. Soc.*, **1936**, 342.

¹⁴ Sommelet, *Compt. rend.*, **157**, 852 (1913).

¹⁵ Mayer and Sieglitz, *Ber.*, **55**, 1846 (1922).

¹⁶ Anderson and Short, *J. Chem. Soc.*, **1933**, 485.

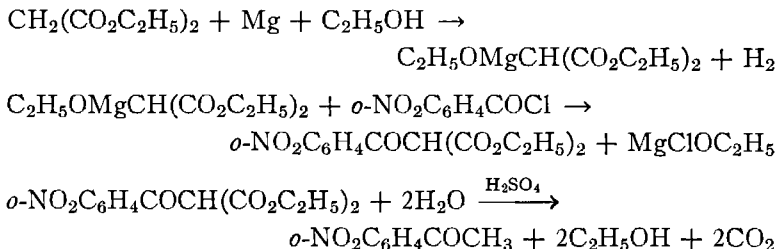
¹⁷ Coles and Dodds, *J. Am. Chem. Soc.*, **60**, 853 (1938).

¹⁸ Rupe and Brentano, *Helv. Chim. Acta*, **10**, 586 (1936).

¹⁹ Ruggli and Preuss, *Helv. Chim. Acta*, **24**, 1350 (1941).

²⁰ Badger, *J. Chem. Soc.*, **1941**, 536.

²¹ Price and Voong, *J. Org. Chem.*, **14**, 115 (1949).

o*-NITROACETOPHENONE*(Acetophenone, *o*-nitro-)**

Submitted by GEORGE A. REYNOLDS and CHARLES R. HAUSER.
 Checked by CLIFF S. HAMILTON and YAO-HUA WU.

1. Procedure

In a 500-ml. three-necked round-bottomed flask equipped with a mercury-sealed stirrer, a dropping funnel, and a reflux condenser (protected by a drying tube) is placed 5.4 g. (0.22 gram atom) of magnesium turnings. Five milliliters (0.085 mole) of absolute ethanol and 0.5 ml. of carbon tetrachloride are added. If the reaction does not start immediately, the flask is heated for a short time on a steam bath. After the reaction has proceeded for several minutes, 150 ml. of absolute ether is added cautiously with stirring. A solution of 35.2 g. (0.22 mole) of diethyl malonate (Note 1), 20 ml. (0.34 mole) of absolute ethanol, and 25 ml. of absolute ether is added with stirring at such a rate that rapid boiling is maintained; heat is supplied when necessary. The mixture is heated under reflux on a steam bath for 3 hours, at which time most of the magnesium has dissolved. To the gray solution is added 37 g. (0.2 mole) of *o*-nitrobenzoyl chloride (Note 2), dissolved in 50 ml. of ether, in a period of 15 minutes. Heating under reflux on the steam bath is continued throughout the addition of the *o*-nitrobenzoyl chloride and until the green solution becomes too viscous to stir. The reaction mixture is cooled and shaken with dilute sulfuric acid (25 g. of concentrated sulfuric

acid in 200 ml. of water) until all the solid has dissolved (Note 3).

The ether phase is separated and the aqueous layer extracted with 75 ml. of ether. The ether extracts are combined and washed with water, and the solvent is removed by distillation.

To the crude diethyl *o*-nitrobenzoylmalonate is added a solution of 60 ml. of glacial acetic acid, 7.6 ml. of concentrated sulfuric acid, and 40 ml. of water, and the mixture is heated under reflux for 4 hours (Note 4) or until no more carbon dioxide is evolved. The reaction mixture is chilled in an ice bath, made alkaline with 20% sodium hydroxide solution, and extracted with several portions of ether. The combined ethereal extracts are washed with water and dried with anhydrous sodium sulfate followed by Drierite, and the solvent is removed by distillation. On fractional distillation of the residue, 27.0–27.4 g. (82–83%) of light-yellow *o*-nitroacetophenone boiling at 158–159°/16 mm. is obtained (n_D^{25} 1.548, n_D^{20} 1.551, d_4^{25} 1.236) (Note 5).

2. Notes

1. The checkers found that the yield of final product was cut in half unless the commercial grade of diethyl malonate was purified by distillation.

2. The *o*-nitrobenzoyl chloride can be prepared from the commercially available acid and thionyl chloride.

3. The solution of the magnesium complex, which is difficult to decompose, is facilitated by mechanical shaking of the mixture for 30 minutes.

4. The decarboxylation is almost complete within 2 to 3 hours.

5. *p*-Nitroacetophenone may be prepared in 73% yield by a similar procedure. Various other methyl ketones have been prepared by this procedure.¹

3. Methods of Preparation

This procedure is an adaptation of one described by Walker and Hauser.¹ Schofield and Swain² state that, in their opinion, for both convenience and economy, this method¹ is the best yet described for the preparation of *o*-nitroacetophenone.²

o-Nitroacetophenone has also been prepared by the treatment of ethyl *o*-nitrobenzoylacetoacetate with sulfuric acid in ethanol,³ by the direct nitration of acetophenone,^{4,5} and by the reaction of *o*-nitrobenzaldehyde with diazomethane.⁶

¹ Walker and Hauser, *J. Am. Chem. Soc.*, **68**, 1386 (1946).

² Schofield and Swain, *J. Chem. Soc.*, **1948**, 384.

³ Kermack and Smith, *J. Chem. Soc.*, **1929**, 814.

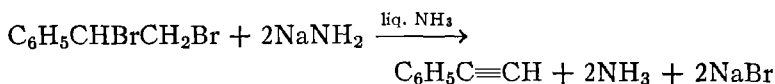
⁴ Morgan and Moss, *J. Soc. Chem. Ind. London*, **42**, 461 (1923).

⁵ Elson, Gibson, and Johnson, *J. Chem. Soc.*, **1930**, 1128.

⁶ Arndt, *Z. angew. Chem.*, **40**, 1099 (1927).

PHENYLACETYLENE

(Benzene, ethynyl-)



Submitted by KENNETH N. CAMPBELL and BARBARA K. CAMPBELL.

Checked by R. S. SCHREIBER and H. E. CUPERY.

1. Procedure

Caution! Avoid contact with styrene dibromide, which is a skin irritant. This preparation should be conducted in a hood to avoid exposure to ammonia.

A 5-l. three-necked flask is equipped with a high-speed, motor-driven stirrer passing through a bushing in the center neck (Note 1). The side necks are equipped with rubber stoppers each carrying a short length of 8-mm. glass tubing, bent at right angles. A 10-12 in. length of stout, flexible iron wire is passed through one

of these pieces of tubing. Two liters of liquid ammonia (Note 2) and 2 g. of ferric nitrate hydrate are placed in the flask. One hundred grams of sodium (4.35 gram atoms) is cut into rectangular pieces about 3 by $\frac{3}{4}$ by $\frac{3}{4}$ in. in size. One of the pieces of sodium is hooked onto the lower end of the iron wire and lowered into the liquid ammonia. Stirring is not necessary during this part of the reaction, but it is advisable. When the lump of sodium has reacted, the solution turns from blue to gray, and the remaining pieces of sodium are added in the same manner. The addition requires about 45 minutes (Note 3).

The stopper carrying the iron wire is removed, 2 g. of aniline is added, and then 528 g. (2 moles) of finely powdered, dry styrene dibromide is added gradually with vigorous stirring. The addition requires about 1 hour (Note 4). Stirring is continued for 2 hours (Note 5) after the addition is completed, after which 600 ml. of concentrated ammonium hydroxide is added, followed by 1 l. of distilled water, and the mixture is allowed to stand until the frost on the outside of the flask is entirely melted.

The aqueous solution is then steam-distilled from the same flask (Note 6) until no more oil passes over. This usually requires about 6 hours, and 1.5-2 l. of distillate is collected. The phenylacetylene in the distillate is separated and washed several times with distilled water to remove ammonia (Note 7). The washed material is dried over anhydrous magnesium sulfate and distilled through an efficient column (Note 8) under reduced pressure. Almost the entire product distils at $73-74^{\circ}/80$ mm. The yield is 93-106 g. (45-52%); n_D^{20} 1.5465-1.5484.

2. Notes

1. A suitable stirrer has been described earlier.¹
2. Additional liquid ammonia should be added from time to time. Liquid ammonia can be handled satisfactorily in fairly large amounts in an open flask, as the frost that quickly forms on the outside of the flask slows down evaporation.
3. This is an excellent method for making sodium amide for many purposes. If the sodium amide is to be used in another

solvent, the solvent should be added to the liquid ammonia after the sodium amide is prepared; the ammonia is allowed to evaporate, and the last traces of ammonia are expelled by heating the flask on a steam bath.

4. The styrene dibromide must not be added too rapidly, or the heat of reaction may cause rapid boiling of the ammonia and possible loss of part of the mixture.

5. In one run this stirring period was increased to 2.8 hours, which resulted in an 11% increase in yield.

6. Because the large amount of ammonia that comes over may entrain considerable phenylacetylene, a very efficient cooling system² is essential.

7. If acid is used to remove the ammonia, the product is likely to be dark colored.

8. The checkers used an 18-in. column packed with Berl saddles.

3. Methods of Preparation

Phenylacetylene has been prepared by treatment of β -bromostyrene with potassium hydroxide³ and with sodium amide in liquid ammonia,⁴ and from styrene dibromide by treatment with sodium amide in liquid ammonia.⁵

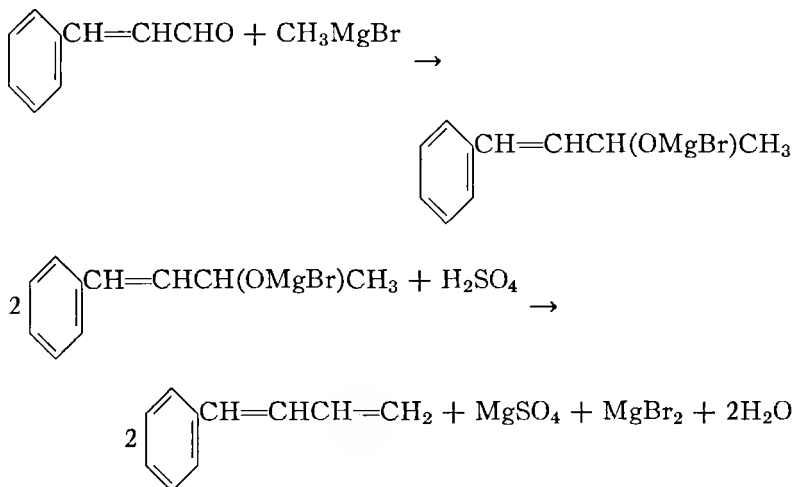
¹ *Org. Syntheses* Coll. Vol. **1**, 34 (1941).

² *Org. Syntheses* Coll. Vol. **2**, 89 (1943).

³ *Org. Syntheses* Coll. Vol. **1**, 438 (1941).

⁴ Vaughn, Vogt, and Nieuwland, *J. Am. Chem. Soc.*, **56**, 2120 (1934).

⁵ Campbell and O'Connor, *J. Am. Chem. Soc.*, **61**, 2898 (1939).

trans-1-PHENYL-1,3-BUTADIENE**(1,3-Butadiene, 1-phenyl-, trans-)**

Submitted by OLIVER GRUMMITT and ERNEST I. BECKER.
 Checked by CHARLES C. PRICE and T. L. PATTON.

1. Procedure

In a 1-l. three-necked flask equipped with a mercury-sealed stirrer, a reflux condenser protected with a calcium chloride drying tube, a separatory funnel, a nitrogen inlet tube, and a thermometer, is placed 0.515 mole of methylmagnesium bromide in 250-350 ml. of ether (a 1.5-2.0 *N* solution). The mixture is cooled to a temperature below 10° by means of an ice-water bath, the stirrer is started, and a solution of 66.1 g. (0.50 mole) of cinnamaldehyde (Note 1) in 60 ml. of absolute ether is added, the rate of addition being controlled so that the temperature is kept below 10°. Throughout the addition, which takes about 1 hour, a slow stream of dry nitrogen is passed through the flask (Note 2).

The flask is detached from the condenser and stirrer, and its contents are transferred to a 500-ml. separatory funnel. The ap-

paratus is then reassembled, without the nitrogen inlet tube or the drying tube, and 175 ml. of 30% sulfuric acid (by weight) is placed in the flask. Without cooling, but with efficient stirring with a Hershberg Nichrome wire stirrer at 1500-1700 r.p.m. (Note 3),¹ the ethereal solution of the cinnamaldehyde-methylmagnesium bromide adduct is added rapidly to the acid. The time for this addition (5-7 minutes) is limited by the efficiency of the condenser. Heat then is applied to maintain gentle reflux until the *total* time elapsed from the initiation of hydrolysis is 20 minutes. The contents of the flask are *immediately* transferred to a 1-l. separatory funnel, the lower aqueous layer is discarded, and the ether layer is washed successively with 50 ml. of water, a mixture of 50 ml. of 5% aqueous sodium hydroxide and 50 ml. of saturated ammonium chloride solution, and 50 ml. of water. Before each of the washings the air in the separatory funnel is displaced with nitrogen. When the second wash solution is added, 0.3 g. of phenyl- β -naphthylamine is dissolved in the ether layer. The washed solution is dried with 20 g. of anhydrous sodium sulfate for 30 minutes and then with 15 g. of anhydrous potassium carbonate for 12 hours.

The ethereal solution is filtered and concentrated by distillation from a steam bath to a residual volume of 80-100 ml. Some water separates at this time, and the mixture is cooled and then dried with about 15 g. of anhydrous potassium carbonate. The concentrated solution is filtered into a 125-ml. modified Claisen flask² and distilled under reduced pressure in a nitrogen atmosphere into a receiver containing 0.3 g. of phenyl- β -naphthylamine. In this manner 52-54 g. (80-83%) of crude *trans*-1-phenyl-1,3-butadiene is obtained, b.p. 81-85°/10-11 mm.; n_D^{25} 1.606-1.608, which may contain some methylstyrylcarbinol and water. This material is dried with 5 g. of anhydrous potassium carbonate, filtered, and distilled as before. The yield of *trans*-1-phenyl-1,3-butadiene is 47-49 g. (72-75%), b.p. 78-81°/8 mm.; n_D^{25} 1.607-1.608. This product is satisfactory for most purposes (Notes 4 and 5).

2. Notes

1. Cinnamaldehyde obtained from the Eastman Kodak Company was purified by washing a solution in an equal volume of ether with aqueous sodium carbonate and then with water, dried, and distilled under nitrogen; b.p. 101–102°/2–3 mm.; n_D^{20} 1.6195.

2. The procedure may be altered at this point so that *trans*-methylstyrylcarbinol is obtained. It is necessary, however, to observe the precaution that all apparatus coming in contact with the *trans*-methylstyrylcarbinol be free from traces of acid.

The solution is stirred for 30 minutes after the addition is complete. Then 125 ml. of a saturated solution of ammonium chloride (about 28%), which has been neutralized to litmus with concentrated ammonium hydroxide, is added dropwise, the temperature being held at 5–10°. This addition takes from 1 to 1.5 hours. After decanting the ether layer, breaking up the precipitate and extracting it with two 60-ml. portions of absolute ether, and adding the extracts to the main solution, the solution is distilled from a steam bath until the residual volume is about 100 ml. The solution is transferred to a Claisen flask, and the residual ether is removed by evacuation with a water pump. After the discard of a small fore-run, the product is collected at 93–94°/1.5 mm.; yield, 65–67 g. (88–90%).

Upon cooling at 0–10° the *trans*-methylstyrylcarbinol forms a mass of white crystals melting at 30–34°. These may be purified by crystallization from petroleum ether (b.p. 30–35°)-methylene chloride (6:1). For each 30 g. of the carbinol, 350 ml. of the solvent mixture is used. The solution is cooled to –75° to –80° in Dry Ice and kept at that temperature for about 3 hours. The solution is filtered quickly by suction through a chilled funnel, washed with the cold solvent mixture, and dried in a vacuum desiccator. The yield of pure *trans*-methylstyrylcarbinol is 28.5 g., m.p. 33.5–34.5°; n_D^{35} 1.5598; d_4^{35} 0.9995.

3. The stirring must be vigorous in order to mix the ether and aqueous layers. This is absolutely essential for the production of reasonable yields. Slower stirring necessitates a longer time for the hydrolysis with consequent longer contact time between

the 1-phenyl-1,3-butadiene and the sulfuric acid, which results in extensive polymerization of the product and corresponding decrease in yield.

4. Pure *trans*-1-phenyl-1,3-butadiene was obtained by distillation of the twice-distilled product under nitrogen through a 12-plate column of the total reflux-variable takeoff type¹ after adding 0.5% of phenyl- β -naphthylamine. The packed section of the column was an 18-in. section of Pyrex tubing (10 mm. o.d.) filled with 4-mm. single-turn glass helices. Insulation was provided by means of a vacuum jacket, and heat losses were compensated by resistance wire wound on the jacket.

About 50% of the sample taken was collected, b.p. 86°/11 mm.; n_D^{25} 1.6086–1.6090; d_4^{25} 0.9235–0.9239.

5. Present evidence indicates that 1-phenyl-1,3-butadiene³ prepared by this method is the *trans* isomer.⁴

3. Methods of Preparation

1-Phenyl-1,3-butadiene has been prepared by the decarboxylation of allocinnamylideneacetic acid⁵ and of cinnamylidenemalononic acid;⁶ the dehydration of methylstyrylcarbinol from the Grignard addition of methylmagnesium halide to cinnamaldehyde,⁷ the rearrangement and dehydration of the alcohol intermediate formed by the Grignard addition of phenylmagnesium bromide to crotonaldehyde,⁸ the formation of methylstyrylcarbinol, its conversion to methylstyrylcarbonyl chloride, and dehydrohalogenation;⁹ a modified Wurtz reaction in which benzyl chloride is coupled with allyl chloride by means of sodium in liquid ammonia;¹⁰ and the condensation of styrene and acetaldehyde and dehydration of the intermediate in the presence of sulfuric acid in acetic acid.¹¹ Reference 11 describes the preparation of 1-phenyl-1,3-butadiene by pyrolysis of 1-phenyl-1,3-butylene-glycol diacetate and 2,6-dimethyl-4-phenyl-1,3-dioxane. The present method is a modification of the procedure of von der Heide.⁷

trans-Methylstyrylcarbinol has been prepared by several methods: the hydrolysis of the addition product formed from

methylmagnesium halide and cinnamaldehyde in a variety of ways;^{9,12} hydrolysis of the addition compound formed from styrylmagnesium bromide and acetaldehyde;³ hydrolysis and hydrogenation of the product formed in the Grignard reaction of phenylethynylmagnesium bromide and acetaldehyde;¹³ the addition of hypobromous acid to 1-phenyl-1,3-butadiene followed by reduction with sodium amalgam in acetic acid;¹⁴ the allylic rearrangement of 1-phenyl-1-acetoxy-3-butene to 1-phenyl-3-acetoxy-1-butene followed by saponification;¹⁵ and the reduction of benzalacetone by means of aluminum isopropoxide.¹⁶ The method employed here is essentially that of Kenyon, Partridge, and Phillips.¹²

¹ *Org. Syntheses* Coll. Vol. **2**, 117 (1943).

² *Org. Syntheses* Coll. Vol. **1**, 130, Fig. 9b (1941).

³ Wright, *J. Org. Chem.*, **1**, 457 (1936).

⁴ Grummitt and Christoph, *J. Am. Chem. Soc.*, **71**, 4157 (1949).

⁵ Liebermann and Riiber, *Ber.*, **33**, 2400 (1900); Doebner and Staudinger, *Ber.*, **36**, 4318 (1903).

⁶ Liebermann and Riiber, *Ber.*, **35**, 2696 (1902); Riiber, *Ber.*, **37**, 2272 (1904); Doebner and Schmidt, *Ber.*, **40**, 148 (1907).

⁷ von der Heide, *Ber.*, **37**, 2101 (1904); Klages, *Ber.*, **37**, 2301 (1904); von Auwers and Eisenlohr, *J. prakt. Chem.*, [2] **84**, 42 (1911); Muskat and Herrman, *J. Am. Chem. Soc.*, **53**, 252 (1931); Flood, Hladky, and Edgar, *Ind. Eng. Chem.*, **25**, 1234 (1933); Briegleb and Kambeitz, *Z. physik. Chem.*, **32B**, 305 (1936).

⁸ Blumenfeld, *Ber.*, **74B**, 524 (1941).

⁹ Klages, *Ber.*, **35**, 2649 (1902); Muskat and Herrman, *J. Am. Chem. Soc.*, **53**, 252 (1931).

¹⁰ Kharasch, Nudenberg, and Fields, *J. Am. Chem. Soc.*, **66**, 1276 (1944).

¹¹ Emerson, *J. Org. Chem.*, **10**, 464 (1945).

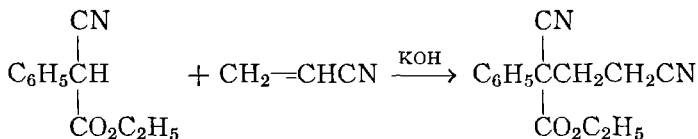
¹² Kenyon, Partridge, and Phillips, *J. Chem. Soc.*, **1936**, 85.

¹³ Campbell, Campbell, and McGuire, *Proc. Indiana Acad. Sci.*, **50**, 87 (1940) [*C. A.*, **35**, 5872 (1941)].

¹⁴ Ingold and Smith, *J. Chem. Soc.*, **1931**, 2752.

¹⁵ Burton, *J. Chem. Soc.*, **1929**, 455.

¹⁶ Lund, *Kem. Maanedstidn.*, **17**, 169 (1936) [*Chem. Zentr.*, **108 I**, 3480 (1937)]. See also Wilds, *Organic Reactions*, **2**, 214, John Wiley & Sons, New York, 1944.

α -PHENYL- α -CARBETHOXYGLUTARONITRILE**(Butyric acid, α,γ -dicyano- α -phenyl-, ethyl ester)**

Submitted by E. C. HORNING and A. F. FINELLI.

Checked by WILLIAM S. JOHNSON and H. WYNBERG.

1. Procedure

In a 500-ml. three-necked flask equipped with a stirrer, a dropping funnel, and a thermometer is placed a solution of 57.0 g. (0.30 mole) of ethyl phenylcyanoacetate¹ in 80 ml. of *tert.*-butyl alcohol. The solution is heated to 40°, and with stirring the dropwise addition of a solution of 33.0 g. (0.62 mole) of acrylonitrile (Note 1) in 30 ml. of *tert.*-butyl alcohol is started. After the addition of about 10–15 drops, 1.0 ml. of a 30% solution of potassium hydroxide in methanol is added, and the temperature is maintained at 40–45° by occasional external cooling while the remaining solution is added slowly. When about one-half of the acrylonitrile has been added, an additional 1.0 ml. of the potassium hydroxide solution is added to ensure the presence of a basic catalyst throughout the reaction. When the addition is completed (after about 30 minutes) and the temperature is no longer maintained above 40° by the exothermic reaction (another 30 minutes), the mixture is heated with a hot-water bath to keep the temperature at 40–45° for 1 hour.

The solution is diluted with 250 ml. of water and acidified with 30–40 ml. of 10% hydrochloric acid. The product is separated after the addition of 100 ml. of ether, and the aqueous solution is extracted with two 50-ml. portions of ether. The combined extracts are washed with 50 ml. of water and dried over anhydrous magnesium sulfate. The ether is distilled at atmospheric pres-

sure, and the residue is distilled under reduced pressure through a short (15-cm.) Vigreux column. After a fore-run of a few grams, the product is collected at 157–167°/0.5 mm. (Note 2). The yield is 50–61 g. (69–83%).

2. Notes

1. The acrylonitrile should be distilled before use. Acrylonitrile vapors are toxic, and the distillation as well as the subsequent reaction should be carried out in a hood.

2. Other observed boiling points are 165–167°/1 mm., 195–200°/6 mm. The product is a colorless, viscous oil, n_D^{25} 1.5100–1.5103.

3. Methods of Preparation

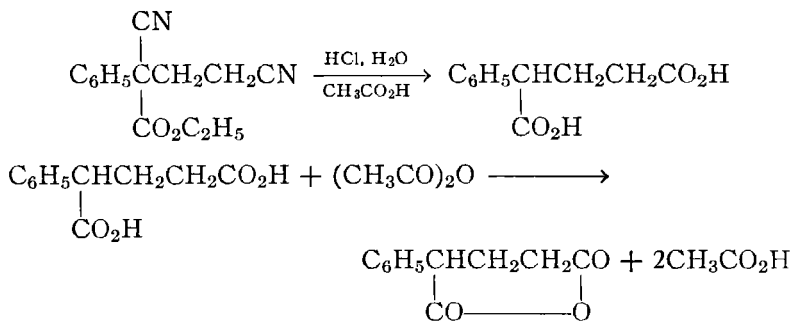
This compound has not been described in the literature previously. The method of preparation follows the general method described by Bruson² for the cyanoethylation of arylacetonitriles.

¹ *Org. Syntheses*, **30**, 43 (1950).

² Bruson and Riener, *J. Am. Chem. Soc.*, **65**, 25 (1943).

α -PHENYLGLUTARIC ANHYDRIDE

(Glutaric anhydride, α -phenyl-)



Submitted by E. C. HORNING and A. F. FINELLI.

Checked by WILLIAM S. JOHNSON and H. WYNBERG.

1. Procedure

In a 500-ml. flask equipped with a reflux condenser are placed 48.4 g. (0.20 mole) of α -phenyl- α -carbethoxyglutaronitrile,¹ 225 ml. of hydrochloric acid (sp. gr. 1.19), and 50 ml. of acetic acid. The mixture is heated under reflux for 10 hours. The solution is cooled, transferred to a 1-l. separatory funnel, and diluted with 300 ml. of water. The α -phenylglutaric acid is extracted with five 100-ml. portions of ether-ethyl acetate (1:1) (Note 1). The extracts are combined, washed once with saturated sodium chloride solution, and dried over anhydrous magnesium sulfate. The solvents are removed as completely as possible by distillation from a steam bath, and the residue is transferred to a 200-ml. flask. Acetic anhydride (50 ml.) is added, and the solution is heated under gentle reflux for 1 hour. The excess acetic anhydride is removed by distillation at atmospheric pressure, and the residue is distilled under reduced pressure through a short (15-cm.) Vigreux column with an air-cooled side arm. The product is collected at 178–188°/0.5–1 mm. (Note 2). The yield is 31.1–32.7 g. (82–86%); m.p. 90–94°.

This material may be recrystallized by dissolving the product in hot ethyl acetate (2 ml. per g. of the anhydride) and adding an equal volume of hexane or 60–68° petroleum ether slowly to the hot solution. The solution is allowed to cool, and when crystallization occurs (usually at 40–50°) an additional volume (2 ml. per g. of the anhydride) of hexane is added. The mixture is cooled, and the crystalline product is removed by filtration and washed with cold hexane (5 ml. per g. of the anhydride). The recovery of colorless material, m.p. 95–96°, is 90–92%.

2. Notes

1. The extraction may be facilitated by saturation of the aqueous layer with sodium chloride.

2. It is necessary to flame the column and side arm. The product obtained in this way is a light-yellow or cream-colored solid which need not be recrystallized unless a colorless sample is de-

sired. If the final distillation is carried out too slowly or at pressures above 2 mm. considerable decomposition may occur, reducing the yield of the product.

3. Methods of Preparation

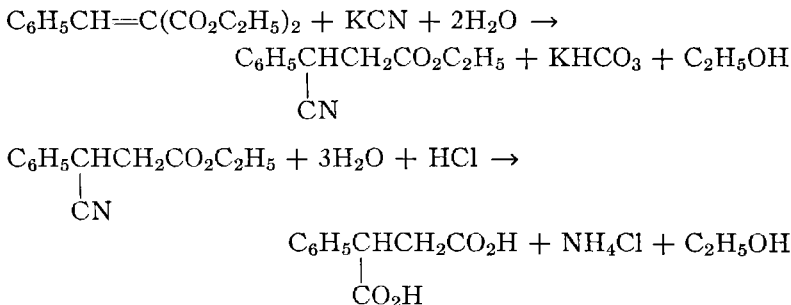
α -Phenylglutaric acid has been prepared previously by the hydrolysis and decarboxylation of diethyl α -phenyl- α -carbethoxyglutarate (prepared by the alkylation of diethyl phenylmalonate with ethyl β -iodopropionate) with hydrochloric acid.² The anhydride may be obtained from the acid by direct distillation under reduced pressure, although the use of acetic anhydride results in a purer product.

¹ *Org. Syntheses*, **30**, 80 (1950).

² Fichter and Merckens, *Ber.*, **34**, 4175 (1901).

PHENYLSUCCINIC ACID

(Succinic acid, phenyl-)



Submitted by C. F. H. ALLEN and H. B. JOHNSON.

Checked by H. R. SNYDER, D. J. MANN, and LEONARD E. MILLER.

1. Procedure

A. *Ethyl β -phenyl- β -cyanopropionate*. In a 5-l. round-bottomed three-necked flask suspended in an oil bath and fitted with a mechanical stirrer, a reflux condenser, and a 250-ml. dropping funnel is placed a solution of 200 g. (0.806 mole) of diethyl benzalmalonate¹ in 2 l. of absolute ethanol. The stirrer is started, and a solution of 56 g. (0.87 mole) of potassium cyanide in 100 ml. of water is added rapidly from the separatory funnel; a small amount of the potassium cyanide precipitates. The temperature of the oil bath is raised to 70° and maintained at 65–75° for 18 hours.

The mixture is cooled to 15°, and the precipitated potassium bicarbonate is collected on a Büchner funnel. The solid (weight 70–72 g.) is washed on the funnel with 100 ml. of 95% ethanol. The combined filtrate and wash liquor is transferred to a 5-l. round-bottomed flask and made slightly acid (*Caution!* Note 1) with dilute hydrochloric acid (about 15–20 ml. of the 10% acid is required). The solution is then concentrated under reduced pressure to a semi-solid residue (Note 1). The cooled residue is shaken with a mixture of 300 ml. of water and 500 ml. of ether. The material dissolves completely; the water layer is separated and washed with 200 ml. of ether. The ether solutions are combined, dried over 20 g. of calcium chloride, filtered into a 2-l. round-bottomed flask equipped with a glass joint, and concentrated by distillation (heating on a steam bath). The crude ethyl β -phenyl- β -cyanopropionate remains as a clear red oil weighing 130–140 g. It is sufficiently pure for use in the next step (Note 2).

B. *Phenylsuccinic acid*. To the crude ester obtained above is added 500 ml. of concentrated hydrochloric acid (sp. gr. 1.19). The flask is fitted to a condenser (Note 3), and the mixture is heated under reflux for 18 hours (Note 4). At the end of this time only a small amount of red oil remains (Note 5). The mixture is cooled, and the nearly solid cake which forms is broken up and collected on a glass filter cloth (Note 5). The crude tan-colored phenylsuccinic acid is washed with 300 ml. of cold water and

dried at 60°. It then weighs 105–110 g. (67–70%) and melts at 163–164° (Notes 6 and 7).

2. Notes

1. Since hydrogen cyanide may be liberated during the acidification and the subsequent concentration, both operations should be carried out in a well-ventilated hood.

2. The pure ester can be obtained by distillation under reduced pressure (b.p. 161–164°/8 mm.).

3. Glass-jointed equipment is required in this step. The flask with a glass joint was used in the preceding operation only to avoid the necessity of transferring the product after the evaporation.

4. Hydrogen chloride is evolved during the first part of the refluxing; it may be disposed of by absorption in water in a gas trap.²

5. The red, oily impurity usually distributes itself as a film on the surface of the liquid and as a lump at the bottom of the flask. It solidifies on cooling and is most conveniently removed as a solid; the thin crust on the surface is lifted with a spatula, and the lump at the bottom of the flask is left undisturbed when the product is collected on the filter.

6. The pure acid can be obtained by recrystallization from water. For each 10 g. of acid about 300 ml. of water and 0.5 g. of Norit are required. The recovery is 85–90% of pure white acid melting at 165.5–166°.

7. The checkers found the product at this stage to be of sufficient purity for conversion to phenylsuccinic anhydride.

3. Methods of Preparation

The preparative methods for phenylsuccinic acid have been listed in an earlier volume.³ The procedure given above is more economical of time and materials than that previously published.³ Applications of the present method, due originally to Brecht and Kallen,⁴ have been published in more recent literature.^{5, 6}

¹ *Org. Syntheses*, **25**, 42 (1945).

² *Org. Syntheses Coll. Vol. 2*, 4 (1943).

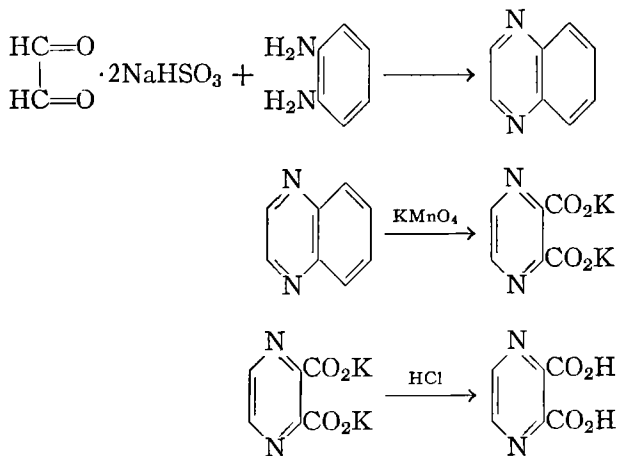
³ *Org. Syntheses Coll. Vol. 1*, 451 (1941).

⁴ Bredt and Kallen, *Ann.*, **293**, 344 (1896).

⁵ Verkade and Hartman, *Rec. trav. chim.*, **52**, 945 (1933).

⁶ Wideqvist, *Arkiv Kemi, Mineral. Geol.*, **14B**, No. 19, 6 pp. (1940) [*C. A.*, **35**, 3993 (1941)].

2,3-PYRAZINEDICARBOXYLIC ACID



Submitted by REUBEN G. JONES and KEITH C. McLAUGHLIN.

Checked by H. R. SNYDER and R. E. HECKERT.

1. Procedure

A. *Quinoxaline*. One hundred thirty-five grams (1.25 moles) of *o*-phenylenediamine ¹ is dissolved in 2 l. of water, and the solution is heated to 70°. With stirring, a solution of 344 g. (1.29 moles) of glyoxal-sodium bisulfite ² (Note 1) in 1.5 l. of hot water (about 80°) is added to the *o*-phenylenediamine solution. The mixture is allowed to stand for 15 minutes and then is cooled to about room temperature and 500 g. of sodium carbonate monohydrate (Note 2) is added. The quinoxaline separates as an oil or as a crystalline solid if the mixture is sufficiently cool. The

mixture is extracted with three 300-ml. portions of ether. The combined extracts are dried over anhydrous magnesium sulfate or sodium sulfate, filtered, and concentrated on the steam bath. The residual liquid, consisting of almost pure quinoxaline, is distilled under reduced pressure, and the fraction boiling at 108–111°/12 mm. (m.p. 29–30°) is collected. It weighs 138–147 g. (85–90%) (Note 3).

B. *2,3-Pyrazinedicarboxylic acid*. A 12-l. three-necked flask is provided with an efficient mechanical stirrer, a reflux condenser, and a 1-l. dropping funnel. In the flask are placed 4 l. of hot (about 90°) water and 145 g. (1.12 moles) of quinoxaline. With rapid stirring a saturated aqueous solution of 1050 g. (6.6 moles) of potassium permanganate (Note 4) is added through the dropping funnel in a thin stream. The rate of addition of the permanganate solution is adjusted so that the reaction mixture boils gently. The addition requires about 1.5 hours.

The reaction mixture is cooled somewhat (Note 5) and filtered through a large Büchner funnel. The manganese dioxide cake is removed from the funnel and stirred to a smooth paste with 1 l. of fresh water. The slurry is filtered, and the washing is repeated. The total filtrate, about 10 l., is evaporated under reduced pressure on the steam bath to a volume of approximately 3 l. (Note 6). The solution is swirled or stirred gently while 550 ml. (6.6 moles) of 36% hydrochloric acid is cautiously added (Note 7). Evaporation under reduced pressure is then continued until a moist cake of solid potassium chloride and 2,3-pyrazinedicarboxylic acid remains in the flask (Note 8).

The moist cake is scraped from the flask and allowed to dry in a 16-in. porcelain evaporating dish until the odor of hydrochloric acid is faint (about 24 hours, but this time can be reduced to about 8 hours if a gentle stream of air is directed onto the solid). The solid material is returned to the dried flask and mixed thoroughly with about 200 ml. of water. Two liters of acetone is added, and the mixture is boiled under reflux for 15 minutes, then cooled to room temperature and filtered through a 6-in. Büchner funnel. The solid on the filter is returned to the flask, treated with 100 ml. of water, and extracted with 1 l. of boiling acetone as before

(Note 9). The acetone filtrates are combined and distilled from a steam bath, finally under diminished pressure.

The solid in the flask is dissolved by refluxing with 2.5 l. of acetone. The mixture is cooled slightly, treated with 10 g. of decolorizing carbon, refluxed for an additional 5-minute period, and filtered hot. Evaporation of the pale yellow acetone filtrate leaves the acid as a light-tan crystalline solid. If the product still possesses an odor of hydrochloric acid it is dried in a vacuum desiccator over sodium hydroxide pellets for a few hours. Finally the product is dried in an oven at 100° for several hours (Notes 10 and 11). The yield of material melting at 165–167° (dec.) is 140–145 g. (75–77%) (Note 12).

If a purer product is desired the material may be recrystallized (with about 17% loss) from 150 ml. of water; the hot solution is decolorized with carbon. The melting point after drying at 110° for several hours is then 183–185° (dec.) (Notes 11 and 13).

2. Notes

1. In the absence of sodium bisulfite, aqueous glyoxal solutions react with *o*-phenylenediamine to give only about 30% yields of quinoxaline together with large quantities of resinous by-products. Therefore, if an aqueous glyoxal solution is to be used in this preparation it should be mixed with a water solution of two molar equivalents of sodium bisulfite before it is added to the *o*-phenylenediamine solution.

2. Potassium carbonate or sodium hydroxide may also be used.

3. 2-Methylquinoxaline may be prepared in 88–92% yields from *o*-phenylenediamine and pyruvic aldehyde-sodium bisulfite by this same procedure.

4. The volume of this solution can be held to the minimum, about 3–5 l., by dissolving the permanganate in hot water (90–100°).

5. The only reason for cooling is to make the flask easier to handle during the filtration.

6. A 5-l. round-bottomed flask fitted with a separatory funnel for continuous addition of the solution during the concentration is convenient.

7. There is a vigorous evolution of carbon dioxide, and unless the acid is added slowly the contents of the flask may foam over.

8. Excess hydrochloric acid is present, and the 2,3-pyrazine-dicarboxylic acid tends to darken and decompose if it is heated too strongly or for too long a time.

9. The ease with which the dicarboxylic acid is removed from the potassium chloride depends upon the amount of water present. The potassium chloride should be set aside for an additional extraction if the yield of the crude product is low.

10. Drying at 100° converts any of the hydrated 2,3-pyrazine-dicarboxylic acids to the anhydrous form.

11. The product darkens somewhat on heating.

12. 2-Methyl-5,6-pyrazinedicarboxylic acid may be prepared in 70-75% yields from 2-methylquinoxaline by this same procedure. The crude acid (m.p. 155-160°, dec.) is somewhat unstable at elevated temperatures. It should not be heated above 100° for long periods of time. In order to obtain pure 2-methyl-5,6-pyrazinedicarboxylic acid (m.p. 175°, dec.) the crude product is best recrystallized from acetone.

13. The melting point is dependent on the rate of heating and the temperature of the bath at the time the sample is inserted. The figure given was obtained by insertion of the sample tube into a bath at 160°.

3. Methods of Preparation

Quinoxaline has been prepared by the reaction of glyoxal with *o*-phenylenediamine,³ and 2-methylquinoxaline by the reaction of pyruvic aldehyde⁴ or isonitrosoacetone⁵ with *o*-phenylenediamine. 2,3-Pyrazinedicarboxylic acid has been prepared only by the permanganate oxidation of quinoxaline.⁶ 2-Methyl-5,6-pyrazinedicarboxylic acid has been prepared from 2-methylquinoxaline in the same way.^{5,7}

¹ *Org. Syntheses Coll. Vol. 2*, 501 (1943).

² *Org. Syntheses*, **24**, 61 (1944).

³ Billman and Rendall, *J. Am. Chem. Soc.*, **66**, 540 (1944).

⁴ Fischer and Taube, *Ber.*, **57**, 1502 (1924).

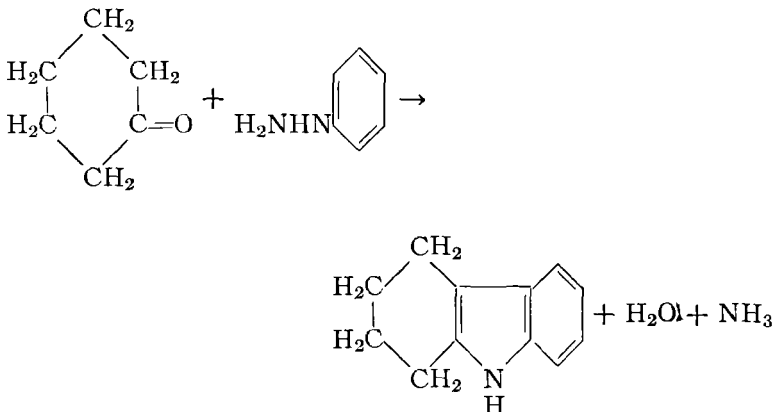
⁵ Böttcher, *Ber.*, **46**, 3084 (1913).

⁶ Gabriel and Sonn, *Ber.*, **40**, 4850 (1907); Sausville and Spoerri, *J. Am. Chem. Soc.*, **63**, 3153 (1941).

⁷ Leonard and Spoerri, *J. Am. Chem. Soc.*, **68**, 526 (1946).

1,2,3,4-TETRAHYDROCARBAZOLE

(Carbazole, 1,2,3,4-tetrahydro-)



Submitted by CROSBY U. ROGERS and B. B. CORSON.

Checked by CHARLES C. PRICE, KENNETH N. CAMPBELL, and ROBERT P. KANE.

1. Procedure

A mixture of 98 g. (1 mole) (Note 1) of cyclohexanone and 360 g. (6 moles) of acetic acid contained in a 1-l. three-necked round-bottomed flask equipped with a reflux condenser, a slip-sealed stirrer, and a dropping funnel is heated under reflux and stirred while 108 g. (1 mole) of phenylhydrazine is added during 1 hour. The mixture is heated under reflux for an additional hour and poured into a 1.5-l. beaker and stirred by hand (Note 2) while it solidifies. It is then cooled to about 5° and filtered with suction,

the filtrate being cooled in ice and refiltered through the filter cake. The final filtrate is discarded. The filter cake is washed with 100 ml. of water and finally with 100 ml. of 75% ethanol. Each wash is allowed to soak into the filter cake before it is sucked dry. The crude solid is air-dried overnight (Note 3) and crystallized (Note 4) from 700 ml. of methanol after treatment with decolorizing carbon (Note 5); yield 120-135 g. of 1,2,3,4-tetrahydrocarbazole, m.p. 115-116° (Note 6). The mother liquor is concentrated to one-fourth of its original volume and yields an additional 10 g. of product (total yield 76-85%) (Note 7).

2. Notes

1. Equivalent amounts of cyclohexanone (after suitable compensation for purity) and phenylhydrazine are used. The cyclohexanone was about 90% pure (analyzed by the procedure of Bryant and Smith¹). Instead of analyzing the ketone, it is safe to assume 90% purity.

2. The stirring should be sufficiently vigorous to prevent the formation of lumps.

3. The crude product requires 50-70 hours of air-drying to attain constant weight (145-155 g., 85-91%). It is preferable to crystallize the partially dried product.

4. The approximate solubility of 1,2,3,4-tetrahydrocarbazole in 100 ml. of methanol at 10°, 35°, and 55° is 5, 12, and 18 g. respectively.

5. A heated funnel is desirable for filtration of the hot solution, for the product separates on slight cooling.

6. The capillary melting point of tetrahydrocarbazole ranges from 113° to 114° with slow heating and from 116° to 118° with fast heating.

7. 1,2-Benzo-3,4-dihydrocarbazole may be prepared by the same general procedure. A solution of 172 ml. (2 moles) of concentrated hydrochloric acid (sp. gr. 1.18) in 500 ml. of water is heated at the reflux temperature and stirred in a 2-l. three-necked round-bottomed flask equipped with a reflux condenser, a slip-sealed stirrer, and a dropping funnel while 108 g. (1 mole) of

phenylhydrazine is added during 5 minutes. α -Tetralone ^{2,3} (146 g., 1 mole or a correspondingly larger amount of material of 90% purity; see Note 1) is added in a period of 1 hour, and the mixture is stirred and heated under reflux for an additional hour. The product is cooled to room temperature with stirring, and the bead-like product is filtered, washed as above, and crystallized from 2.3 l. of methanol after treatment with decolorizing carbon. The first crop amounts to 105-110 g. and the second crop to 75-80 g., making the total yield 82-87%; m.p. 163-164°.

3. Methods of Preparation

1,2,3,4-Tetrahydrocarbazole has been prepared from cyclohexanone phenylhydrazone,^{4,5,6,7,8,9} by the direct reaction of cyclohexanone with phenylhydrazine,¹⁰ and by the hydrogenation of carbazole.¹¹ 1,2-Benzo-3,4-dihydrocarbazole has been prepared from the phenylhydrazone of α -tetralone¹² and by the direct reaction of α -tetralone with phenylhydrazine.¹⁰

¹ Bryant and Smith, *J. Am. Chem. Soc.*, **57**, 57 (1935).

² *Org. Syntheses* Coll. Vol. **2**, 569 (1943).

³ *Org. Syntheses*, **20**, 94 (1940).

⁴ Frechsel, *J. prakt. Chem.*, [2] **38**, 69 (1888).

⁵ Baeyer, *Ann.*, **278**, 88 (1893); Baeyer and Tutein, *Ber.*, **22**, 2178 (1889).

⁶ Borsche, *Ann.*, **359**, 49 (1908).

⁷ Perkin and Plant, *J. Chem. Soc.*, **119**, 1825 (1921).

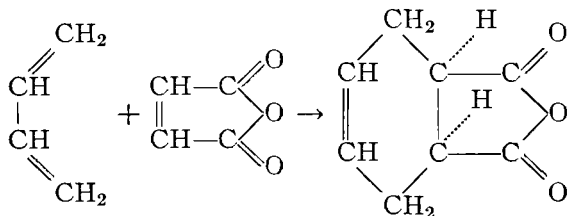
⁸ Hoshino and Takiura, *Bull. Chem. Soc. Japan*, **11**, 218 (1936) [*C. A.*, **30**, 5985 (1936)].

⁹ Grammaticakis, *Compt. rend.*, **209**, 317 (1939).

¹⁰ Rogers and Corson, *J. Am. Chem. Soc.*, **69**, 2910 (1947).

¹¹ Adkins and Coonradt, *J. Am. Chem. Soc.*, **63**, 1563 (1941).

¹² Ghigi, *Gazz. chim. ital.*, **60**, 194 (1930).

cis- Δ^4 -TETRAHYDROPHTHALIC ANHYDRIDE**(4-Cyclohexene-1,2-dicarboxylic anhydride, *cis*-)**

Submitted by ARTHUR C. COPE and ELBERT C. HERRICK.

Checked by CHARLES C. PRICE, KENNETH N. CAMPBELL, and ROBERT P. KANE.

1. Procedure

The apparatus shown in Fig. 3, consisting of a 2-l. three-necked round-bottomed flask fitted with an efficient stirrer (Note 1), a gas inlet tube, a thermometer, and a reflux condenser is assembled in a ventilated hood. Bubblers tubes containing benzene are attached to the gas inlet tube and the top of the reflux condenser, and 500 ml. of dry benzene and 196 g. (2 moles) of maleic anhydride (Note 2) are placed in the flask. Stirring is begun, the flask is heated with a pan of hot water, and butadiene is introduced (from a commercial cylinder controlled by a needle valve) at a rapid rate (0.6–0.8 l. per minute). When the temperature of the solution has reached 50° (within 3–5 minutes) the pan of water is removed. The exothermic reaction causes the temperature to reach 70–75° in 15–25 minutes. The rapid stream of butadiene is nearly completely absorbed for 30–40 minutes, after which the rate is decreased until the reaction is completed (equal rates of bubbling in the two bubbler tubes) after 2–2.5 hours. The solution is poured into a 1-l. beaker at once to avoid crystallization of the product in the reaction flask. The beaker is covered and the mixture is kept at 0–5° overnight.

The product is collected on a large Büchner funnel and washed with 250 ml. of 35–60° petroleum ether. A second crop (5–15 g.)

obtained by diluting the filtrate with an additional 250 ml. of petroleum ether is separated by filtration, combined with the first crop in a large crystallizing dish, and dried to constant weight

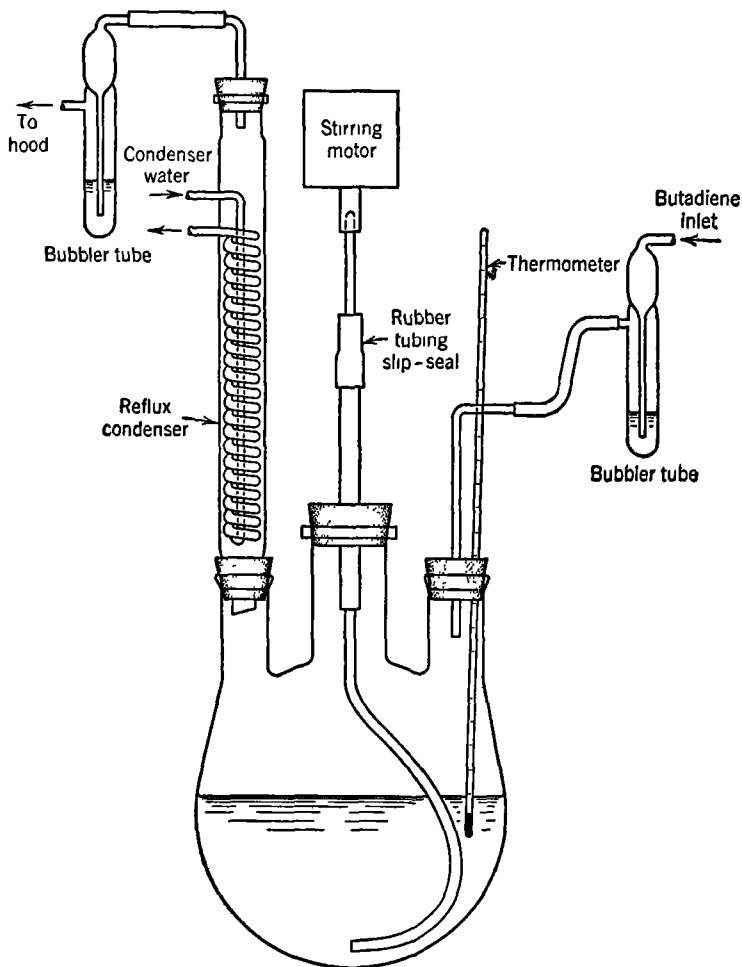


FIG. 3. Assembly of apparatus for addition of butadiene to maleic anhydride

(1-2 hours) in an oven at 70-80°. The yield of *cis*- Δ^4 -tetrahydrophthalic anhydride is 281.5-294.5 g. (93-97%), m.p. 99-102° (Note 3).

2. Notes

1. Any stirrer that produces sufficiently vigorous agitation to disperse the gas through the liquid is satisfactory. It was found to be unnecessary to introduce the gas below the surface of the liquid.

2. A good grade of commercial maleic anhydride was used, m.p. 52–54°.

3. The product is analytically pure and suitable for use in preparing diethyl *cis*- Δ^4 -tetrahydrophthalate. Recrystallization from ligroin ¹ or ether ² raises the m.p. to 103–104°.

3. Methods of Preparation

cis- Δ^4 -Tetrahydrophthalic anhydride has been prepared by the reaction of maleic anhydride and butadiene.^{1,2,3,4,5} The procedure described is adapted from the one used by Kohler and Jansen.⁴

¹ Diels and Alder, *Ann.*, **460**, 113 (1928).

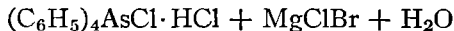
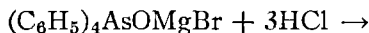
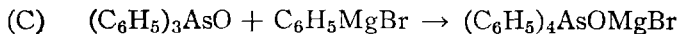
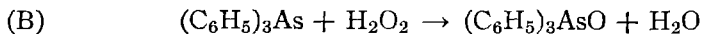
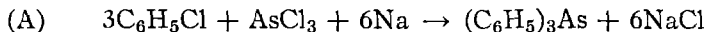
² Jenkins and Costello, *J. Am. Chem. Soc.*, **68**, 2733 (1946).

³ Farmer and Warren, *J. Chem. Soc.*, **1929**, 903

⁴ Kohler and Jansen, *J. Am. Chem. Soc.*, **60**, 2144 (1938).

⁵ Fieser and Novello, *J. Am. Chem. Soc.*, **64**, 806 (1942).

TETRAPHENYLARSONIUM CHLORIDE HYDROCHLORIDE



Submitted by R. L. SHRINER and CALVIN N. WOLF.

Checked by CLIFF S. HAMILTON and YAO-HUA WU.

1. Procedure

Caution! All steps in the following preparations should be performed under a hood, since volatile arsenic compounds may be liberated.

A. *Triphenylarsine*. In a 2-l. round-bottomed three-necked flask is placed 130 g. (5.65 gram atoms) of powdered sodium¹ covered with 900 ml. of benzene. The flask is fitted with an Allihn condenser, a mercury-sealed mechanical Hershberg stirrer, and a 500-ml. dropping funnel in which is placed a mixture of 170 g. (0.94 mole) of arsenic trichloride and 272 g. (2.42 moles) of chlorobenzene. About 10 ml. of the arsenic trichloride-chlorobenzene mixture is dropped into the flask, and the reaction mixture is stirred and heated on a steam bath until it darkens and boils spontaneously. The steam bath is removed, and the remainder of the arsenic trichloride-chlorobenzene mixture is added dropwise, with stirring, over a period of 1–1.5 hours at such a rate that gentle boiling is maintained (Note 1). When the addition is complete, the mixture is stirred and heated under reflux on a steam bath for 12 hours.

The reaction mixture is filtered while hot through a large Büchner funnel, and the filtrate is collected in a 3-l. filter flask. The residue (Note 2) is washed on the funnel with two 200-ml. portions of hot benzene, pressed as dry as possible, and then transferred to a 1-l. beaker, boiled with 300 ml. of benzene, and filtered, the same funnel and flask being used. This extraction process is repeated twice.

The combined benzene filtrates are subjected to distillation from a steam bath to remove the benzene. The flask containing the residual red oil is connected to a water pump and heated under reduced pressure in an oil bath at 110–120° for 2 hours to remove unreacted starting materials. When cooled, the crude triphenylarsine solidifies to a light brown solid which melts at 57–59°. The yield is 230–240 g. (93–97%). The crude product is dissolved in 650–700 ml. of hot 95% ethanol and placed in a refrigerator overnight. The crystals are collected on a Büchner funnel and washed

with 50 ml. of cold 95% ethanol. The yield is 218–225 g. (88–91%) of white crystals which melt at 61°.

B. *Triphenylarsine oxide*. In a 500-ml. round-bottomed flask equipped with a mechanical stirrer, a thermometer, and a 100-ml. dropping funnel is placed 100 g. (0.33 mole) of the recrystallized triphenylarsine (Note 3) dissolved in 200 ml. of acetone. To the solution 46 g. (0.41 mole) of 30% hydrogen peroxide is added dropwise, with stirring, over a period of 20–30 minutes. A water-ice bath is used to maintain the temperature at 25–30°. When the addition is complete, stirring is continued for 30 minutes, and the acetone is then removed by distillation.

The flask containing the residual yellow oil is fitted with a water trap and condenser, and 120 ml. of benzene is added. The water is then removed by azeotropic distillation (Note 4). When the removal of water is complete, the triphenylarsine oxide is crystallized by cooling the flask in an ice bath for 1.5–2 hours. The light-brown crystals are collected on a Büchner funnel and washed on the funnel with 25 ml. of cold benzene. The crude product weighs 97–98.5 g. (91–93%) and melts at 186–188°. The crude product is transferred to a porcelain dish and triturated with 50 ml. of benzene, collected on a Büchner funnel, pressed as dry as possible, and washed with 25 ml. of cold benzene. After drying in the air, the triphenylarsine oxide amounts to 89–92 g. (84–87%) of white crystals, melting at 189°.

C. *Tetraphenylarsonium chloride hydrochloride*. In a 2-l. round-bottomed three-necked flask fitted with a condenser, a mercury-sealed mechanical Hershberg stirrer, and a dropping funnel is placed 40 g. (0.124 mole) of triphenylarsine oxide dissolved in 1 l. of hot benzene. To this solution there is added with vigorous stirring a solution of phenylmagnesium bromide which is prepared from 34.6 g. (0.22 mole) of bromobenzene, 6.0 g. (0.25 gram atom) of magnesium, and 200 ml. of dry ether. A brown viscous solid separates. The mixture is stirred for 15 minutes and then stirred and heated under reflux on a steam bath for 30 minutes. The solvent is removed by decantation, and the viscous solid is washed with 500 ml. of benzene. The addition product is

then hydrolyzed with 100 ml. of water containing 5 ml. of concentrated hydrochloric acid.

The hydrolysis mixture is transferred to a 1-l. round-bottomed flask fitted with a reflux condenser, and 500 ml. of concentrated hydrochloric acid is added (Note 5). The mixture is heated on a steam bath for 1.5–2 hours. The flask is cooled in an ice bath; the crystals are collected on a sintered-glass funnel and washed with 200 ml. of ice-cold concentrated hydrochloric acid and then with 200 ml. of ice-cold dry ether. The crude product weighs 50–56 g. The product is dissolved in a mixture of 50 ml. of water and 150 ml. of concentrated hydrochloric acid by boiling under reflux. The tetraphenylarsonium chloride hydrochloride separates when the solution is cooled in an ice bath. The white needles are collected on a sintered-glass funnel and washed with 50 ml. of ice-cold concentrated hydrochloric acid and then with 200 ml. of ice-cold dry ether. The yield of tetraphenylarsonium chloride hydrochloride melting at 204–208° with decomposition is 42–45 g. (74–80%).

2. Notes

1. If the addition of the arsenic trichloride-chlorobenzene mixture is too rapid, the reaction becomes vigorous and must be moderated with a cooling bath.

2. Before being discarded, the residue should be treated with ethanol to destroy unreacted sodium.

3. If crude triphenylarsine is used, the final product is difficult to purify.

4. Triphenylarsine oxide is partly converted to the dihydroxide when heated with water. However, it is not hygroscopic under ordinary conditions.²

5. The hydrolysis product consists mainly of tetraphenylarsonium bromide, which is converted to tetraphenylarsonium chloride hydrochloride by crystallization from concentrated hydrochloric acid.

3. Methods of Preparation

Triphenylarsine has been prepared by the action of arsenic triiodide³ or arsenic trichloride⁴ on phenylmagnesium bromide

and by the action of sodium and arsenic trichloride on chlorobenzene⁵ or bromobenzene.⁶ The method described here is essentially that of Pope and Turner.⁵

Triphenylarsine oxide has been prepared by the action of sodium hydroxide on triphenylarsine dibromide,⁷ by the action of potassium permanganate on triphenylarsine,⁸ and by the action of hydrogen peroxide on triphenylarsine.⁹ The method described here is essentially that of Vaughan and Tarbell.⁹

Tetraphenylarsonium chloride hydrochloride has been prepared by the action of phenylmagnesium bromide on triphenylarsine oxide.¹⁰ The method described here is essentially that of Blicke and Monroe.¹⁰

¹ *Org. Syntheses Coll. Vol. 1*, 252 (1941).

² Blicke and Cataline, *J. Am. Chem. Soc.*, **60**, 419 (1938).

³ Burrows and Turner, *J. Chem. Soc.*, **117**, 1373 (1920).

⁴ Pfeiffer and Pietsch, *Ber.*, **37**, 4621 (1904).

⁵ Pope and Turner, *J. Chem. Soc.*, **117**, 1447 (1920).

⁶ Michaelis, *Ann.*, **321**, 160 (1902).

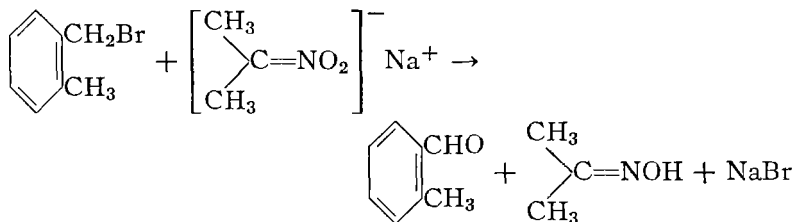
⁷ Phillips, *Ber.*, **19**, 1031 (1886).

⁸ Blicke and Safir, *J. Am. Chem. Soc.*, **63**, 575 (1941).

⁹ Vaughan and Tarbell, *J. Am. Chem. Soc.*, **67**, 144 (1945).

¹⁰ Blicke and Monroe, *J. Am. Chem. Soc.*, **57**, 720 (1935).

o-TOLUALDEHYDE



Submitted by H. B. HASS and MYRON L. BENDER.

Checked by ARTHUR C. COPE and MALCOLM CHAMBERLAIN.

1. Procedure

Eleven and one-half grams (0.50 gram atom) of sodium is dissolved in 500 ml. of absolute ethanol in a 1-l. round-bottomed

flask. Forty-six grams (0.52 mole) of 2-nitropropane is added, then 92.5 g. (0.50 mole) of *o*-xylyl bromide (Note 1). The flask is attached to a reflux condenser connected to a drying tube and shaken at intervals for 4 hours. The reaction mixture, originally at room temperature, becomes warm spontaneously, and a white precipitate of sodium bromide forms (Note 2).

After a reaction period of 4 hours the sodium bromide is separated by filtration and the ethanol is removed by distillation on a steam bath. The residue of product and sodium bromide is dissolved in 100 ml. of ether and 150 ml. of water. The ether layer is washed with two 50-ml. portions of 10% sodium hydroxide solution to remove any acetoxime and excess 2-nitropropane and is then washed with 50 ml. of water. The ether layer is separated and is dried with 15 g. of anhydrous sodium sulfate, and the ether is removed by distillation on a steam bath.

The crude product is distilled from a Claisen flask under reduced pressure. The yield of *o*-tolualdehyde boiling at 68–72°/6 mm., n_D^{25} 1.5430, is 41–44 g. (68–73%) (Note 3).

2. Notes

1. *o*-Xylyl bromide may be obtained from the Eastman Kodak Company or may be prepared by the light-catalyzed bromination of *o*-xylene.¹

2. The solution is originally supersaturated with the sodium salt of 2-nitropropane, and a precipitate of this salt may be mistaken for sodium bromide.

3. This is a general method for the preparation of substituted benzaldehydes. The following aldehydes have been prepared by the same general procedure.²

ALDEHYDE	YIELD, %
<i>p</i> -Bromobenzaldehyde	75
Benzaldehyde	73
<i>p</i> -Carbomethoxybenzaldehyde	72
<i>p</i> -Cyanobenzaldehyde	70
<i>p</i> Trifluoromethylbenzaldehyde	77

3. Methods of Preparation

A procedure for the preparation of *o*-tolualdehyde from *o*-toluanilide by the Sonn-Müller method has been published in *Organic Syntheses*.³ In addition to the alternative methods of preparation listed there, *o*-tolualdehyde has been prepared from *o*-xylyl bromide and hexamethylenetetramine,⁴ by the Stephen reduction of *o*-tolunitrile,⁵ and by the procedure of the present preparation.²

¹ Cumming, Hopper, and Wheeler, *Systematic Organic Chemistry*, p. 351, Constable and Company, London, 1937 (description of a procedure for light-catalyzed bromination which is applicable to *o*-xylene).

² Hass and Bender, *J. Am. Chem. Soc.*, **71**, 1767 (1949).

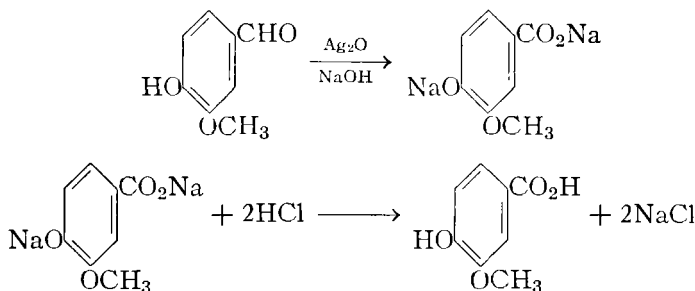
³ *Org. Syntheses*, **26**, 97 (1946).

⁴ Sommelet, *Compt. rend.*, **157**, 852 (1913).

⁵ Stephen, *J. Chem. Soc.*, **127**, 1874 (1925).

VANILLIC ACID

I. SILVER OXIDE METHOD



Submitted by IRWIN A. PEARL.

Checked by R. L. SHRINER and CALVIN N. WOLF.

1. Procedure

A solution of 170 g. (1.0 mole) of silver nitrate in 1 l. of water in a 2-l. beaker is treated, with stirring, with a solution of 44 g. (1.07 moles) of 97% sodium hydroxide in 400 ml. of water (Note

1). The mixture is stirred for 5 minutes, and the silver oxide is collected on an 11-cm. Büchner funnel with suction and washed free of nitrates with water (Note 2). The wet, freshly precipitated silver oxide is transferred to a 4-l. beaker (Note 1), covered with 2 l. of water, and treated with 200 g. (4.85 moles) of 97% sodium hydroxide pellets with vigorous stirring. If the temperature of the mixture at this point is below 55°, the mixture is warmed to 55–60°. With continued stirring at 55–60° (Note 3), 152 g. (1.0 mole) of vanillin (Note 4) is added; the reaction begins after a few minutes. The silver oxide is transformed to fluffy metallic silver, and considerable heat is evolved. Stirring is continued for 10 minutes, the mixture is filtered, and the precipitated silver is washed with 100 ml. of hot water. A rapid stream of sulfur dioxide gas (Note 5) is passed into the combined filtrate and washings for 2 minutes, and the resulting solution is poured into 1.1 l. of 1:1 hydrochloric acid with vigorous stirring. The resulting mixture, which should be acid to Congo red, is cooled to 15–20°. The vanillic acid is collected on a Büchner funnel, pressed to remove the mother liquor, washed with 150 ml. of ice water (Note 6), sucked as dry as possible, and air-dried. The yield is 140–160 g. (83–95%) of white needles melting at 209–210°. This product is pure enough for most purposes, but it may be purified by recrystallization from water containing a little sulfur dioxide, 1.2 l. of water being used per 100 g. of product. Pure white needles melting at 210–211° are obtained with a recovery of 90–97%.

2. Notes

1. This reaction should be performed in glass apparatus with a glass stirrer. If stainless steel is employed, the resulting vanillic acid may be dark in color.

2. The presence of nitrates in the solution will cause the formation of nitro acids when the final acidification takes place.

3. Fifty to fifty-five degrees was found to be the critical temperature for this reaction. If the reactants are mixed cold, heat must be applied to raise the temperature above 50°, at which

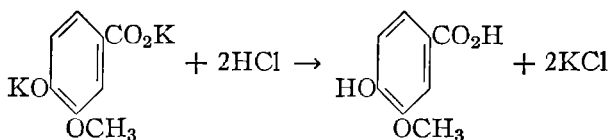
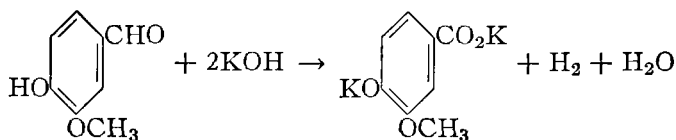
point the reaction begins. Mixing of the reactants at temperatures much higher than 60° results in a violent reaction.

4. Commercial u.s.p. vanillin is satisfactory.

5. The treatment with sulfur dioxide prevents the product from becoming tan in color.

6. Extraction of the combined filtrate and washings with three 200-ml. portions of ether, followed by removal of the ether by distillation, yields an additional 4-20 g. of product melting at 206-208°. It may be purified by recrystallization from water containing a little sulfur dioxide to give white needles melting at 209-210°.

II. CAUSTIC FUSION METHOD



Submitted by IRWIN A. PEARL.

Checked by R. L. SHRINER and ROBERT C. JOHNSON.

1. Procedure

In a stainless-steel beaker of approximately 2-l. capacity (120 mm. by 165 mm.) equipped with an efficient mechanical Ni-chrome or Monel stirrer (Note 1) and heated by an electric hot plate are placed 178 g. (4.3 moles) of 97% sodium hydroxide pellets, 178 g. (2.7 moles) of 85% potassium hydroxide pellets (Note 2), and 50 ml. of water. The mixture is stirred and heated to 160°, at which temperature the hot plate is turned off. Twen-

ty-five grams of vanillin is added. The temperature drops somewhat, and after a very short time a vigorous reaction begins which raises the temperature to 180–195°. An additional 127 g. (total of 1.0 mole) of vanillin is gradually added to the reaction mixture during a period of 10–12 minutes at a rate sufficient to maintain the reaction temperature (Note 3). After all the vanillin is added, stirring is continued for 5 minutes. The hot plate is removed, and the mixture is allowed to cool with stirring. When the mixture cools to about 150–160°, 1 l. of water is added and the mixture is stirred until all the fusion mixture is dissolved. The solution is transferred to a 4-l. beaker, 500 ml. of water being used to rinse the stirrer and metal beaker. Sulfur dioxide gas is introduced for 1 minute (Note 4), and the reaction mixture is cooled to room temperature. The mixture is acidified with about 1.2 l. of 6 *N* hydrochloric acid using Congo red as the indicator and keeping the mixture cool during addition of the acid by stirring and cooling in an ice bath. The mixture is cooled, and the light-tan precipitate is filtered, washed with 150 ml. of ice water, and dried. The yield of vanillic acid melting at 206–208° is 150–160 g. (89–95%) (Note 5). The product can be recrystallized from water, using 1.2 l. per 100 g. of vanillic acid. A 90–97% recovery of nearly white vanillic acid melting at 209–210° is obtained.

2. Notes

1. An efficient stirrer can be made from No. 8 Nichrome or Monel metal wire in a rectangular shape of dimensions such that it is about two-thirds the height of the beaker and has a clearance of 1–2 mm. with the sides of the beaker (Fig. 4). A rigid form is maintained by spot-welding the crossed wires. The metal beaker must be firmly clamped. It is important that there should be effective stirring throughout all the reaction mixture in order to prevent caking, excessive local temperature rises, and foaming.

2. The exact proportion of sodium hydroxide to potassium hydroxide is not critical as long as the total amount of alkali is more than 7 moles. Alkali mixtures containing more than 70% sodium

hydroxide are not desirable because they are not as fluid as other mixtures.

3. The temperature of the mixture should not be allowed to rise much above 200° for any length of time because traces of protocatechuic acid will be formed and contaminate the vanillic acid.

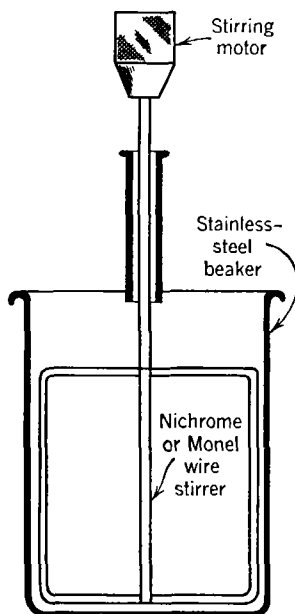


FIG. 4. Apparatus for caustic fusion of vanillin.

4. The sulfur dioxide treatment prevents the product from becoming tan in color.

5. An additional few per cent may be obtained by ether extraction of the filtrate.

3. Methods of Preparation

Vanillic acid has been prepared from vanillin in small amounts by action of moist air,¹ exposure to sunlight and nitrobenzene,² reaction with soil bacteria,³ ozone,⁴ and by caustic fusion.^{5,6} High yields of vanillic acid have been obtained from vanillin by con-

trolled caustic fusion,⁷ oxidation with silver oxide,^{8,9} mercuric oxide,¹⁰ and gold oxide¹⁰ and by the Cannizzaro reaction of vanillin in the presence of a silver catalyst.¹¹ Vanillic acid has been prepared indirectly from vanillin by the hydrolysis of acetylvanillic acid prepared by oxidation with peracetic acid of acetylvanillin,¹² and by the hydrolysis of acetovanillonitrile prepared by the reaction of vanillin oxime with acetic anhydride.¹³ The procedures described are essentially those reported by Pearl.^{7,8}

¹ Tiemann, *Ber.*, **8**, 1134 (1875).

² Ciamician and Silber, *Ber.*, **38**, 3821 (1905).

³ Robbins and Lathrop, *Soil Sci.*, **7**, 475 (1919).

⁴ Dorland and Hibbert, *Can. J. Research*, **18B**, 33 (1940).

⁵ Lock, *Ber.*, **62**, 1187 (1929).

⁶ Sabalitschka and Tietz, *Arch. Pharm.*, **269**, 545 (1931).

⁷ Pearl, *J. Am. Chem. Soc.*, **68**, 2180 (1946).

⁸ Pearl, *J. Am. Chem. Soc.*, **68**, 429 (1946).

⁹ Pearl, *J. Am. Chem. Soc.*, **68**, 1100 (1946).

¹⁰ Pearl, *J. Am. Chem. Soc.*, **67**, 1628 (1945).

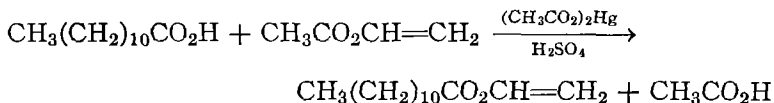
¹¹ Pearl, *J. Org. Chem.*, **12**, 79 (1947).

¹² Böeseken and Greup, *Rec. trav. chim.*, **58**, 528 (1939).

¹³ Raiford and Potter, *J. Am. Chem. Soc.*, **55**, 1682 (1933).

VINYL LAURATE AND OTHER VINYL ESTERS

(Lauric acid, vinyl ester)



Submitted by DANIEL SWERN and E. F. JORDAN, JR.

Checked by WILLIAM S. JOHNSON and LELAND J. CHINN.

1. Procedure

In a 500-ml. round-bottomed three-necked flask provided with a thermometer, a reflux condenser, and a gas inlet tube through which a stream of nitrogen is passed (Note 1) are placed 206 g. (2.4 moles) of freshly distilled vinyl acetate (Note 2) and 80 g. (0.4 mole) of lauric acid (Note 3). The lauric acid is dissolved by

warming, and 1.6 g. of mercuric acetate is added. The mixture is shaken by hand for about 30 minutes, and 0.15 ml. of 100% sulfuric acid is added dropwise (Note 4). The solution is heated under reflux for 3 hours, then 0.83 g. of sodium acetate trihydrate is added to neutralize the sulfuric acid. The excess vinyl acetate is recovered by distillation at atmospheric pressure (vapor temperature about 70–80°) until the pot temperature reaches 125° (Note 5). The distillation is completed at 10 mm. or lower (Note 5), and, after the collection of a small quantity of low-boiling material, fairly pure vinyl laurate (Note 6) is obtained as a colorless liquid, b.p. 142–143°/10 mm. (138–139°/8 mm.; 124–126°/3 mm.). The yield is 50–57 g. (55–63%). Redistillation (Note 7) yields 48–53 g. (53–59%) of pure vinyl laurate, b.p. 142–142.5°/10 mm. (120–120.5°/2 mm.); n_D^{25} 1.4387 (Notes 8 and 9).

2. Notes

1. All operations should be conducted in a nitrogen atmosphere to minimize the formation of polymer.

2. An Eastman Kodak Company practical grade of vinyl acetate is satisfactory. It was distilled immediately before use through a 48 by $\frac{3}{4}$ in. column packed with $\frac{3}{32}$ -in. single-turn Pyrex glass helices. The checkers employed material obtained from the Niacet Chemicals Division, Niagara Falls, New York, distilled once through a 12-in. Vigreux column, b.p. 73°/746 mm.

3. Lauric acid, m.p. 44°, was prepared from the commercial acid obtained from Armour and Company, Chicago, Illinois. The acid was recrystallized twice from acetone at –40° (10 ml. of acetone per gram of acid) and distilled under reduced pressure through a well-insulated, electrically heated 30 by 1 in. column packed with $\frac{1}{4}$ -in. Berl saddles. Pure lauric acid has a boiling point of 167–168°/8 mm. and n_D^{45} 1.4316. The Eastman Kodak Company grade of lauric acid melting at 43–44° is satisfactory.

4. The 100% sulfuric acid is prepared by cautiously adding 7.3 g. of fuming sulfuric acid containing 30% sulfur trioxide to 10 g. of 95% sulfuric acid.

5. An electrically heated 18 by $\frac{1}{2}$ in. Vigreux column was employed.

6. The vinyl laurate, which has an acid number of about 2, usually contains a small quantity of mercury at this stage, from which it can be separated by decantation.

7. Sufficient sodium bicarbonate is added to the pot charge to neutralize the free acid present (see Note 6).

8. Additional properties of vinyl laurate are n_D^{35} 1.4345 and d_4^{30} 0.8639. If the iodine number is determined by the Wijs method, a 200% excess of iodine chloride solution and a 1-hour reaction period should be employed in order to obtain values which are 97–99% of the theoretical value.

9. Vinyl caproate, caprylate, pelargonate, caprate, myristate, palmitate, stearate, 10-hendecenoate (undecylenate) and oleate can be prepared in a similar manner, except that in the preparation of the palmitate and stearate the fatty acids are added to a solution of mercuric acetate and sulfuric acid in vinyl acetate. Vinyl stearate is not redistilled, but the once-distilled product is recrystallized from acetone at 0° (3 ml. of acetone per gram of vinyl stearate). The amount of mercuric acetate employed was 2%, and the amount of 100% sulfuric acid was 0.3–0.4% of the weight of the stearic acid. Average yields and properties of these vinyl esters are given in the table.

VINYL ESTER	YIELD,	BOILING POINT		n_D^{30}	d_4^{30}
	%	°C.	mm.		
Caproate	40	98–99	100	1.4159	0.8837
Caprylate	55	134–135	100	1.4256	0.8719
Pelargonate	55	133–133.5	50	1.4291	0.8689
Caprate	45	148	50	1.4320	0.8670
Myristate	60	147–148	4.8	1.4407	0.8617
Palmitate (m.p. 26.7–27.1°)	35	168–169	4.5	1.4438	0.8602
Stearate (m.p. 35–36°)	30	187–188	4.3	1.4423 (at 40°)	0.8517 (at 40°)
10-Hendecenoate	70	124–124.5	10	1.4442	0.8799
Oleate	60	178	2.8	1.4533	0.8691

The acids used for preparing the vinyl esters tabulated were Eastman Kodak Company pure grade except for the following,

which were obtained from the companies indicated and purified by fractionation through an efficient fractionating column: caproic acid, b.p. $96^{\circ}/8$ mm., Carbide and Carbon Chemicals Corporation, New York; caprylic acid, b.p. $124-125^{\circ}/8$ mm., capric acid, b.p. $145-146^{\circ}/8$ mm., Armour and Company, Chicago, Illinois; pelargonic acid, b.p. $176^{\circ}/64$ mm., Emery Industries, Cincinnati, Ohio; 10-hendecenoic (undecylenic) acid, b.p. $177-180^{\circ}/25$ mm., Baker Castor Oil Company, New York. Oleic acid was prepared from olive-oil fatty acids by low-temperature crystallization and distillation.¹

3. Methods of Preparation

The procedure described is substantially that of Toussaint and MacDowell,² with minor modifications.³ Vinyl esters of long-chain aliphatic acids have also been prepared by the reaction of acetylene with the appropriate acids,^{4,5,6} but this reaction is not so convenient for small-scale laboratory preparations:

¹ Brown and Shinowara, *J. Am. Chem. Soc.*, **59**, 6 (1937); Wheeler and Riemen-schneider, *Oil and Soap*, **16**, 207 (1939).

² Toussaint and MacDowell, U. S. pat. 2,299,862 [*C. A.*, **37**, 1722 (1943)].

³ Swern, Billen, and Knight, *J. Am. Chem. Soc.*, **69**, 2439 (1947); Swern and Jordan, *J. Am. Chem. Soc.*, **70**, 2334 (1948).

⁴ Reppe, Ger. pat. 588,352 [*C. A.*, **28**, 1357 (1934)]; U. S. pat. 2,066,075 [*C. A.*, **31**, 1037 (1937)].

⁵ Imperial Chemical Industries, Brit. pat. 581,501 [*C. A.*, **41**, 2428 (1947)].

⁶ Powers, *Ind. Eng. Chem.*, **38**, 837 (1946).

SUBJECT INDEX

(This index comprises material from Volume 30 only; for previous volumes see Collective Volumes 1 and 2 and Volume 29.)

Names in small capital letters refer to the titles of individual preparations. A page number in bold-face italics indicates that detailed preparative directions are given or referred to; entries so treated include principal products and major by-products, special reagents or intermediates (which may or may not be isolated), compounds mentioned in the text or Notes as having been prepared by the method given, and apparatus described in detail or illustrated by a figure. Page numbers in ordinary type indicate pages on which a compound or subject is mentioned in connection with other preparations. For example, Aniline hydrochloride, 5, 6, indicates that aniline hydrochloride is mentioned on page 5, and that directions for its preparation are given on page 6.

- | | |
|--|--|
| ACETIC ACID, CYANOPHENYL-, ETHYL ESTER, 43 | <i>o</i> -Aminophenol, 57 |
| Acetic anhydride, 82 | 3-AMINOPYRIDINE, 3 |
| ACETONITRILE, CHLORO-, 22 | <i>p</i> -AMINOTETRAPHENYLMETHANE, 5 |
| ACETOPHENONE, <i>o</i> -NITRO-, 70 | <i>p</i> -Aminotetraphenylmethane hydrochloride, 5 |
| 9-ACETYLANTHRACENE, 1 | Ammonia, liquid, 15, 73 |
| Acetyl chloride, 1 | Ammonium hydroxide, 41, 46 |
| Acetylene, 15 | Ammonolysis of diethyl fumarate, 46 |
| Acidolysis of vinyl acetate by fatty acids, 106 | <i>n</i> -Amylacetylene, 17 |
| Acrylonitrile, 80 | Aniline hydrochloride, 5, 6 |
| Addition, of ethyl phenylcyanoacetate to acrylonitrile, 80 | Anthracene, 1 |
| of hydrogen sulfide to methyl acrylate, 65 | Apparatus for alternately evacuating and introducing nitrogen, 19 |
| of hypochlorous acid to cyclopentene, 24 | Arsenic trichloride, 96 |
| of potassium cyanide to diethyl benzalmalonate, 84 | DL-ASPARTIC ACID, 7 |
| Aldehyde-collidine, 42 | Autoclave, use of hydrogenation bomb as, 42 |
| Aldehyde synthesis, from benzyl halides and 2-nitropropane, 99 | Azeotropic distillation, 30, 31 |
| Sommelet, 67 | |
| Alkylation, of acetylene, 15 | Benzaldehyde, 100 |
| of aniline with triphenylcarbinol, 5 | BENZENE, ETHYNYL-, 72 |
| of diethyl phthalimidomalonate, 7 | 2-BENZIMIDAZOLETHIOL, 56 |
| Aluminum chloride, 1, 63 | 1,2-Benzo-3,4-dihydrocarbazole, 91 |
| Amino acid, 7 | Benzophenone, 19 |
| N β -Aminoethylethylenimine, 39 | Benzoyl chloride, 11 |
| β -Aminoethylsulfuric acid, 38 | BENZOYLCHOLINE CHLORIDE, 10 |
| | BENZOYLCHOLINE IODIDE, 10 |
| | Benzoylcholine picrate, 13 |
| | BNLYLAMINI, 2,3-DIMETHOXY-N-METHYL-, 59 |

- Bromine, 3
p-Bromobenzaldehyde, **100**
 Bromobenzene, 97
 α -Bromo-*n*-butyric acid, 62
 α -Bromo-*n*-butyryl chloride, **62**
 Butadiene, 93
 1,3-BUTADIENE, 1-PHENYL-, *trans*-, **75**
 BUTANE, 1,4-DIODO-, **33**
n-BUTYLACETYLENE, **15**
tert.-Butyl alcohol, 19, 20
n-Butyl bromide, 16
n-Butyl iodide, **34**
 BUTYRIC ACID, α,γ -DICYANO- α -PHENYL-,
 ETHYL ESTER, **80**
- CARBAZOLE, 1,2,3,4-TETRAHYDRO, **90**
 β -CARBETHOXY- γ,γ -DIPHENYLVINYLACE-
 TIC ACID, **18**
p-Carbomethoxybenzaldehyde, **100**
 Carbon disulfide, 57
 Chlorine, 24
 Chloroacetamide, 22
 CHLOROACETONITRILE, **22**
 Chlorobenzene, 96
trans-2-CHLOROCYCLOPENTANOL, **24**
 2-Chloroethyl benzoate, **11**
 Chloromethylation, 68
 1-Chloromethylnaphthalene, **67, 68**
 Chlorourea, *see* Monochlorourea
 CHOLINE, CHLORIDE BENZOATE, **10**
 CHOLINE, IODIDE BENZOATE, **10**
 Cinnamaldehyde, 75, 77
 Cleavage of tetrahydrofuran, 27, 33
 Condensation, of aniline and triphenyl
 carbinol, 5
 of diethyl carbonate and phenylaceto-
 nitrile, 43
 of a ketone and diethyl succinate, 18
p-Cyanobenzaldehyde, **100**
 Cyanoethylation of ethyl phenylcyano-
 acetate, 80
 Cyclization, of β -aminoethylsulfuric acid
 to ethylenimine, 38
 1,2-benzo-3,4-dihydrocarbazole from
 phenylhydrazine and α -tetralone,
 91
 5-ethyl-2-methylpyridine synthesis,
 41
- Cyclization, hexahydro-1,3,5-triacyl-*s*-
 triazines from nitriles and formal-
 dehyde, 51
 2-mercaptobenzimidazole from
o-phenylenediamine, 56
 2-mercaptobenzoxazole from *o*-amino-
 phenol, 57
 1-methyl-3-ethyloxindole from
N-methyl- α -bromo-*n*-butyranilide,
 63
 2-methylquinoxaline from *o*-phenyl-
 enediamine, 88
 quinoxaline from *o*-phenylenediamine,
 86
 1,2,3,4-tetrahydrocarbazole from
 phenylhydrazine and cyclohexa-
 none, 90
 1,2-CYCLOHEXANEDICARBOXYLIC ACID,
 DIETHYL ESTER, *cis*-, **29**
 Cyclohexanone, 90
 4-CYCLOHEXENE-1,2-DICARBOXYLIC
 ACID, DIETHYL ESTER, *cis*-, **29**
 4-CYCLOHEXENE-1,2-DICARBOXYLIC AN-
 HYDRIDE, *cis*-, **93**
 CYCLOPENTANOL, 2-CHLORO-, *trans*-, **24**
 Cyclopentene, 25
- Dehydration, of chloroacetamide, 22
 of fumaramide, 46
 of *trans*-methylstyrylcarbinol, 76
 α -phenylglutaric acid to α -phenylglu-
 taric anhydride, 82
 Dehydrohalogenation by sodium amide,
 72
 4,4'-DICHLORODIBUTYL ETHER, **27**
 Diels-Alder reaction of butadiene with
 maleic anhydride, 93
 Diene synthesis of *cis*- Δ^4 -tetrahydro-
 phthalic anhydride, 93
 Diethyl benzalmalonate, 84
 Diethyl carbonate, 44
 Diethyl fumarate, 46
 DIETHYL *cis*-HEXAHYDROPHTHALATE, **29**
 Diethyl malonate, 70
 Diethyl *o*-nitrobenzoylmalonate, **71**
 Diethyl sodium phthalimidomalonate,
 7
 Diethyl succinate, 19

- DIETHYL *cis*- Δ^4 -TETRAHYDROPHTHALATE, 29
- Dihydropyran, 48
- 1,4-DIODOBUTANE, 33
- 2,3-Dimethoxybenzaldehyde, 60
- Dimethyl fumarate, 47
- Dimethyl *cis*-hexahydrophthalate, 32
- Dimethyl *cis*- Δ^4 -tetrahydrophthalate, 31
- Esterification by azeotropic distillation with toluene, 30, 31
- Ester interchange between vinyl acetate and fatty acids, 106
- 1,2-ETHANEDITHIOL, 35
- Ethanol, 30, 44
- ETHER, *bis*(4-CHLOROBUTYL), 27
- Ethyl chloroacetate, 7
- Ethylene chlorohydrin, 11
- Ethylene dibromide, 35
- Ethylene diisothiuronium bromide, 36
- ETHYLENIMINE, 38
- toxic properties of, 40
- 5-ETHYL-2-METHYLPYRIDINE, 41
- ETHYL PHENYLGLYANOACETATE, 43, 80
- Ethyl β -phenyl- β -cyanopropionate, 84
- Extractor, continuous, 4
- Fischer indole synthesis, of 1,2-benzo-3,4-dihydrocarbazole, 91
- of 1,2,3,4-tetrahydrocarbazole, 90
- Formaldehyde, 51
- Friedel-Crafts reaction, 1
- Fumaramide, 46
- FUMARONITRILE, 46
- Fusion, caustic, of vanillin, 103
- GLUTARIC ACID, 48
- GLUTARIC ANHYDRIDE, α -PHENYL, 81
- Glyoxal-sodium bisulfite, 86
- Grignard reaction, *trans*-methylstyryl-carbinol, 77
- tetraphenylarsonium chloride hydrochloride, 97
- Hexahydro-1,3,5-triacetyl-*s* triazine, 52
- Hexahydro-1,3,5 triacrylyl *s* triazine, 52
- Hexahydro-1,3,5-tribenzoyl-*s*-triazine, 52
- Hexahydro-1,3,5-tri(β -chloropropionyl)-*s*-triazine, 52
- Hexahydro-1,3,5-trimethacrylyl-*s*-triazine, 52
- HEXAHYDRO-1,3,5-TRIPROPIONYL *s*-TRIAZINE, 51
- Hexamethylenetetramine, 67
- n*-Hexylacetylene, 17
- 1-Hexyne, 15
- Hofmann degradation, 3
- Hydrogenation, of a double bond, 30, 32
- over palladium, 32
- over platinum, 30, 32
- over Raney nickel for reductive alkylation, 60, 61
- Hydrogen peroxide, 97
- Hydrogen sulfide, 65
- Hydrolysis, and decarboxylation of an acylmalonic ester, 71
- and decarboxylation of α -phenyl- α -carbethoxyglutaronitrile, 81
- and decarboxylation of triethyl α -phthalimidoethane α,α,β -tricarboxylate, 8
- of dihydropyran, 48
- of ethyl β -phenyl- β -cyanopropionate, 84
- δ -Hydroxyvaleraldehyde, 48 50
- Iodination of thiophene, 53
- Iodine, 53
- 2-Iodoethyl benzoate, 11
- 2-Iodo-5-nitrothiophene, 55
- 2-iodothiophene, 53
- Isoamylacetylene, 17
- Isopropyl iodide, 34
- KETONE, 9-ANTHRYL METHYL, 1
- Lauric acid, 106
- LAURIC ACID, VINYL ESTER, 106
- Magnesium, 70, 97
- Maleic anhydride, 93
- Malonic ester, ethoxymagnesium derivative, solution of, 70

- Malonic ester synthesis, 7
acylation by *o*-nitrobenzoyl chloride, 70
- 2-MERCAPTOBENZIMIDAZOLE, 56
- 2-Mercaptobenzoxazole, 57
- Methanesulfonic acid, 58
- METHANESULFONYL CHLORIDE, 58
- Methanol, 31
- Methyl acrylate, 65
- Methylamine, 60
- Methylaniline, 62
- N-Methylarylamines, preparation by reductive alkylation, 59, 60
- N-Methyl- α -bromo-*n*-butyranilide, 63
- N-METHYL-2,3-DIMETHOXYBENZYLAMINE, 59
- 1-METHYL-3-ETHYLOXINDOLE, 62
- Methylmagnesium bromide, 75
- 2-Methyl-5,6-pyrazinedicarboxylic acid, 89
- 2-Methylquinoxaline, 88, 89
- trans*-Methylstyrylcarbinol, 77
- METHYL β -THIODIPROPIONATE, 65
- Monochlorourea, 24, 25, 26
- 1-NAPHTHALDEHYDE, 67, 68
- Nicotinamide, 3
- Nitric acid, 48
- o*-NITROACETOPHENONE, 70
- p*-Nitroacetophenone, 71
- o*-Nitrobenzoyl chloride, 70
- 2-Nitropropane, 100
- Oxidation, by nitric acid, 48
of aldehyde to carboxyl group, 49
of hydroxyl to carboxyl group, 49
of 2-methylquinoxaline to 2-methylpyrazine-5,6-dicarboxylic acid, 89
of quinoxaline to 2,3-pyrazinedicarboxylic acid, 87
of triphenylarsine to triphenylarsine oxide, 97
of vanillin, by caustic fusion, 103
by silver oxide, 101
- OXINDOLE, 3-ETHYL-1-METHYL, 62
- Paraldehyde, 41
- Phenylacetonitrile, 44
- PHENYLACETYLENE, 72
- trans*-1-PHENYL-1,3-BUTADIENE, 75
- α -PHENYL- α -CARBETHOXYGLUTARONITRILE, 80, 82
- o*-Phenylenediamine, 56, 86
- α -Phenylglutaric acid, 82
- α -PHENYLGLUTARIC ANHYDRIDE, 81
- Phenylhydrazine, 90
- Phenylmagnesium bromide, 97
- PHENYLSUCCINIC ACID, 83
- Phenylsuccinic anhydride, 85
- Phosphoric acid, ortho-, 33, 34
- Phosphoric anhydride, 33
- Phosphorus oxychloride, 27
- Phosphorus pentoxide, 22, 46
- Potassium, 19, 20
directions for safe handling of, 20
- Potassium *tert*-butoxide, solution of, 19
- Potassium cyanide, 84
- Potassium ethyl xanthate, 56
- Potassium hydroxide, 103
- Potassium iodide, 34
- Potassium permanganate, 87
- PROPIONIC ACID, β , β' -THIODI-, DIMETHYL ESTER, 65
- Propionitrile, 51
- n*-Propylacetylene, 17
- 2,3-PYRAZINEDICARBOXYLIC ACID, 86
- PYRIDINE, 3-AMINO, 3
- PYRIDINE, 5-ETHYL-2-METHYL, 41
- Pyruvic aldehyde-sodium bisulfite, 88
- Quaternary ammonium salt, benzoylcholine chloride and iodide, 10
- Quinoxaline, 86, 87
- Reductive alkylation of methylamine by 2,3-dimethoxybenzaldehyde, 59
- Replacement, bromine by a thiol group, 35
chlorine atom by iodine, 11
- Seal for mechanical stirrer, 54
- Silver chloride, 12
- Silver oxide, 102
- Sodamide, *see* Sodium amide
- Sodium, 15, 44, 73, 96

- Sodium acetylide, solution in liquid ammonia, **15**
Sodium amide, solution of, **73**
Sodium ethoxide, **44, 45**
 solution of, **99**
Sodium hydroxide, **103**
Sodium hypobromite, solution of, **3**
Sodium iodide, **11**
Stirrer, for caustic fusion, **104, 105**
 seal for, **54**
Stobbe condensation, **18**
Styrene dibromide, **73**
SUCCINIC ACID, α -BENZHYDRYLIDENE-,
 α -ETHYL ESTER, **18**
 PHENYL-, **83**
Sulfonyl chloride from sulfonic acid, **58**

1,2,3,4-Tetrahydrocarbazole, **90**
Tetrahydrofuran, **27, 33**
cis- Δ^4 -Tetrahydrophthalic anhydride, **30, 93**
 α -Tetralone, **92**
Tetraphenylarsonium bromide, **98**
TETRAPHENYLARSONIUM CHLORIDE HYDROCHLORIDE, **95**
Thionyl chloride, **58, 62**
Thiophene, **53**
THIOPHENE, 2-iodo-, **53**
Thiourea, **35**
o-Tolualdehyde, **99**

p-Toluenesulfonic acid, **30, 31**
p-Toluidine, α, α, α -triphenyl-, **5**
s-Triazine, hexahydro-1,3,5-tripropionyl-, **51**
Triethyl α -phthalimidoethane- α, α, β -tricarboxylate, **7**
p-Trifluoromethylbenzaldehyde, **100**
Trimethylamine, **12**
Trioxane, **51**
Triphenylarsine, **96**
Triphenylarsine oxide, **97**
Triphenylcarbinol, **5, 6**

Urea, **24**

VANILLIC ACID, **101, 103**
Vanillin, **102, 104**
Vinyl acetate, **106**
Vinyl caprate, **108**
Vinyl caproate, **108**
Vinyl caprylate, **108**
Vinyl 10-hendecenoate, **108**
VINYL LAURATE, **106**
Vinyl myristate, **108**
Vinyl oleate, **108**
Vinyl palmitate, **108**
Vinyl pelargonate, **108**
Vinyl stearate, **108**
Vinyl undecylenate, **108**

o-Xylyl bromide, **100**

NOMENCLATURE

Preparations appear in the alphabetical order of common names of the compounds. For convenience in surveying the literature concerning any preparation through *Chemical Abstracts* subject indexes, the *Chemical Abstracts* indexing name for each compound is given as a subtitle if it differs from the common name used as the title.

SUBMISSION OF PREPARATIONS

Chemists are invited to submit for publication in *Organic Syntheses* procedures for the preparation of compounds which are of general interest or which illustrate useful synthetic methods. The procedures submitted should represent, as nearly as possible, optimum conditions for the preparations, and should have been checked carefully by the submitter. Full details of all steps in the procedure should be included, and the range of yields should be reported rather than the maximum yield obtainable. The melting point of each solid product should be given, and the boiling-point range and refractive index (at 25°) of each liquid product. The method of preparation or source of the reactants and the criteria for the purity of the products should be stated.

Procedures submitted should be written in the style employed in the latest volume of *Organic Syntheses*. Copies of the current style sheet may be obtained upon request from the Secretary of the Editorial Board. Two copies of procedures which are submitted should be sent to the Secretary. Additions, corrections, and improvements to preparations previously published are welcomed and should be sent to the Secretary.

COPYRIGHT, 1950
BY
ORGANIC SYNTHESSES, INC.

All Rights Reserved

*This book, or any part thereof, must not
be reproduced in any form without
the written permission of the publisher.*

PRINTED IN THE UNITED STATES OF AMERICA

CONTENTS

9-ACETYLANTHRACENE	1
3-AMINOPYRIDINE	3
<i>p</i> -AMINOTETRAPHENYLMETHANE	5
DL-ASPARTIC ACID	7
BENZOYLCHOLINE IODIDE AND CHLORIDE	10
<i>n</i> -BUTYLACETYLENE	15
β -CARBETHOXY- γ,γ -DIPHENYLVINYLACETIC ACID	18
CHLOROACETONITRILE	22
<i>trans</i> -2-CHLOROCYCLOPENTANOL	24
4,4'-DICHLORODIBUTYL ETHER	27
DIETHYL <i>cis</i> - Δ^4 -TETRAHYDROPHthalATE AND DIETHYL <i>cis</i> -HEXAHYDRO- PHthalATE	29
1,4-DIODOBUTANE	33
ETHANEDITHIOL	35
ETHYLENIMINE	38
5-ETHYL-2-METHYLPYRIDINE	41
ETHYL PHENYLCYANOACETATE	43
FUMARONITRILE	46
GLUTARIC ACID	48
HEXAHYDRO-1,3,5-TRIPROPIONYL- <i>s</i> -TRIAZINE	51
2-IODOTHIOPHENE	53
2-MERCAPTOBENZIMIDAZOLE	56
METHANESULFONYL CHLORIDE	58
<i>N</i> -METHYL-2,3-DIMETHOXYBENZYLAMINE	59
1-METHYL-3-ETHYLOXINDOLE	62
METHYL β -THIODIPROPIONATE	65
1-NAPHTHALDEHYDE	67
<i>o</i> -NITROACETOPHENONE	70
PHENYLACETYLENE	72
<i>trans</i> -1-PHENYL-1,3-BUTADIENE	75
α -PHENYL- α -CARBETHOXYGLUTARONITRILE	80
α -PHENYLGLUTARIC ANHYDRIDE	81
PHENYLSUCCINIC ACID	83
2,3-PYRAZINEDICARBOXYLIC ACID	86
1,2,3,4-TETRAHYDROCARBAZOLE	90
<i>cis</i> - Δ^4 -TETRAHYDROPHthalIC ANHYDRIDE	93
TETRAPHENYLARSONIUM CHLORIDE HYDROCHLORIDE	95
<i>o</i> -TOLUALDEHYDE	99
VANILLIC ACID	101
VINYL LAURATE AND OTHER VINYL ESTERS	106
INDEX	111

CONTRIBUTORS

Other than members of the Board

KLIEM ALEXANDER	E. F. JORDAN, JR.
S. J. ANGYAL	HENRY Y. LEW
DON M. BALCOM	KEITH C. McLAUGHLIN
ERNEST I. BECKER	CHARLES MERRITT, JR.
MYRON L. BENDER	DAVID T. MOWRY
CHARLES E. BRAUN	IRWIN A. PEARL
JOHN MANN BUTLER	FREDERICK J. PILGRIM
BARBARA K. CAMPBELL	E. EMMET REID
KENNETH N. CAMPBELL	D. B. REISNER
MARVIN CARMACK	EDWARD F. RIENER
B. B. CORSON	GEORGE A. REYNOLDS
J. E. DAYAN	CROSBY U. ROGERS
B. D. DEACON	M. W. RUTENBERG
HUGH B. DONAHOE	HAROLD SCHECHTER
M. S. DUNN	WILLIAM P. SCHNEIDER
J. ENGLISH, JR.	B. W. SMART
EDWARD A. FEHNEL	F. W. SPANGLER
A. F. FINELLI	A. JOHN SPEZIALE
A. H. FORD-MOORE	HERMAN STONE
ROBERT L. FRANK	DANIEL SWERN
M. A. GRADSTEN	W. O. TEETERS
OLIVER GRUMMITT	J. R. TETAZ
H. B. HASS	H. V. TOWLES
CHARLES R. HAUSER	J. A. VAN ALLAN
PETER J. HEARST	CALVIN A. VANDERWERF
ELBERT C. HERRICK	E. R. WEBSTER
H. B. JOHNSON	J. G. WILSON
REUBEN G. JONES	BENJAMIN WITTEN
CALVIN N. WOLF	

ORGANIC SYNTHESSES

AN ANNUAL PUBLICATION OF SATISFACTORY
METHODS FOR THE PREPARATION
OF ORGANIC CHEMICALS

VOLUME 30

1950

ADVISORY BOARD

ROGER ADAMS	R. C. FUSON
C. F. H. ALLEN	HENRY GILMAN
W. E. BACHMANN	W. W. HARTMAN
A. H. BLATT	JOHN R. JOHNSON
H. T. CLARKE	OLIVER KAMM
J. B. CONANT	C. S. MARVEL
N. L. DRAKE	C. R. NOLLER
L. F. FIESER	RALPH L. SHRINER

LEE IRVIN SMITH

BOARD OF EDITORS

ARTHUR C. COPE, *Editor-in-Chief*

RICHARD T. ARNOLD	W. S. JOHNSON
T. L. CAIRNS	CHARLES C. PRICE
C. S. HAMILTON	R. S. SCHREIBER
E. C. HORNING	H. R. SNYDER

NORMAN RABJOHN, *Secretary to the Board*
University of Missouri, Columbia, Missouri

NEW YORK · JOHN WILEY & SONS, INC.

LONDON · CHAPMAN & HALL, LIMITED



werelion@yandex.ru